

***** STN Columbus *****

FILE 'HOME' ENTERED AT 11:06:19 ON 04 APR 2002

=> file biosis,caba,caplus,embase,japio,lifesci,medline,scisearch,uspatfull

=> e smith daniel j/au

E1 1 SMITH DANIEL H/AU
E2 2 SMITH DANIEL I/AU
E3 212 --> SMITH DANIEL J/AU
E4 1 SMITH DANIEL JAMES/AU
E5 1 SMITH DANIEL JOHANNES/AU
E6 6 SMITH DANIEL JOHN/AU
E7 4 SMITH DANIEL JOSEPH/AU
E8 4 SMITH DANIEL K/AU
E9 5 SMITH DANIEL KEITH/AU
E10 4 SMITH DANIEL L/AU
E11 14 SMITH DANIEL M/AU
E12 1 SMITH DANIEL MORRIS JR/AU

=> s e3-e7 and streptoc?

L1 63 ("SMITH DANIEL J"/AU OR "SMITH DANIEL JAMES"/AU OR "SMITH DANIEL
JOHANNES"/AU OR "SMITH DANIEL JOHN"/AU OR "SMITH DANIEL JOSEPH"
/AU) AND STREPTOC?

=> dup rem l1

PROCESSING COMPLETED FOR L1

L2 45 DUP REM L1 (18 DUPLICATES REMOVED)

=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 45 ANSWERS - CONTINUE? Y/(N):y

L2 ANSWER 1 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 2001:886776 CAPLUS

DN 136:36332

TI Synthetic peptide vaccines for dental caries

IN ***Smith, Daniel J.*** ; Taubman, Martin A.

PA USA

SO U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. 5,686,075.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI US 2001048926	A1	20011206	US 1997-967573	19971110
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US 5686075	A	19971111	US 1993-57162	19930430
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PRAI US 1992-877295 B2 19920501

US 1993-57162	A2	19930430
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AB Vaccine compns. and immunogenic compns. are described which are glucosyltransferase subunit vaccines for dental caries and which contain at least one peptide which corresponds to a sequence of glucosyltransferase contg. aspartate 413, aspartate 415 or both aspartate 413 and aspartate 415. These subunit vaccines elicit antibodies which protect an immunized mammal from dental caries. Methods of provoking an immune response to intact glucosyltransferase are also described.

L2 ANSWER 2 OF 45 USPATFULL
AN 2001:223710 USPATFULL
TI SYNTHETIC PEPTIDE VACCINES FOR DENTAL CARIES
IN ***SMITH, DANIEL J.*** , NATICK, MA, United States
TAUBMAN, MARTIN A., NEWTONVILLE, MA, United States
PI US 2001048926 A1 20011206
AI US 1997-967573 A1 19971110 (8)
RLI Continuation-in-part of Ser. No. US 1993-57162, filed on 30 Apr 1993,
GRANTED, Pat. No. US 5686075 Continuation-in-part of Ser. No. US
1992-877295, filed on 1 May 1992, ABANDONED
DT Utility
FS APPLICATION
LREP PATRICIA GRANAHAAN, HAMILTON BROOK SMITH AND REYNOLDS, TWO MILITIA DRIVE,
LEXINGTON, MA, 02173
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN 8 Drawing Page(s)
LN.CNT 804
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Vaccine compositions and immunogenic compositions are described which
are glucosyltransferase subunit vaccines for dental caries and which
contain at least one peptide which corresponds to a sequence of
glucosyltransferase containing aspartate 413, aspartate 415 or both
aspartate 413 and aspartate 415. These subunit vaccines elicit
antibodies which protect an immunized mammal from dental caries. Methods
of provoking an immune response to intact glucosyltransferase are also
described.

L2 ANSWER 3 OF 45 USPATFULL
AN 2001:111865 USPATFULL
TI Chitosan-based nitric oxide donor compositions
IN ***Smith, Daniel J.*** , Stow, OH, United States
Serhatkulu, Sibel, Akron, OH, United States
PA The University of Akron, Akron, OH, United States (U.S. corporation)
PI US 6261594 B1 20010717
AI US 1998-199732 19981125 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Kulkosky, Peter F.
LREP Renner, Kenner, Greive, Bobak, Taylor & Weber
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 689
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A chitosan-based polymeric nitric oxide donor composition comprising a
modified chitosan polymer and a nitric oxide [N2O2] dimer, wherein the
nitric oxide [N2O2] dimer is bonded directly to the backbone of the
modified chitosan polymer without further binding through a nucleophile
residue or moiety. The chitosan-based polymeric nitric oxide donor
composition is capable of site specific delivery and controlled release
of nitric oxide under physiological conditions. The chitosan-based
polymeric nitric oxide donor composition further provides a carrier
having medically beneficial properties. A method is further included for
preparing a chitosan-based polymeric nitric oxide donor composition

comprising reacting a nitric oxide dimer (80-100 p.s.i.) with a modified chitosan polymer in the presence of sodium methoxide at room temperature. The chitosan-based polymeric nitric oxide composition can be incorporated into dry powder inhalers, wound dressings, implants, injectables, condoms, wound dressings and prosthesis coatings for use in a variety of medical applications in which an effective dosage of nitric oxide is indicated as a preferred method of treatment.

L2 ANSWER 4 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

1

AN 2001:543227 BIOSIS

DN PREV200100543227

TI Cloning of the ***Streptococcus*** mutans gene encoding glucan binding protein B and analysis of genetic diversity and protein production in clinical isolates.

AU Mattos-Graner, Renata O.; Jin, Song; King, William F.; Chen, Tsute; ***Smith, Daniel J.*** ; Duncan, Margaret J. (1)

CS (1) Department of Molecular Genetics, Forsyth Institute, 140 Fenway, Boston, MA, 02115: mduncan@forsyth.org USA

SO Infection and Immunity, (November, 2001) Vol. 69, No. 11, pp. 6931-6941. print.

ISSN: 0019-9567.

DT Article

LA English

SL English

AB ***Streptococcus*** mutans, the primary etiological agent of dental caries, produces several activities that promote its accumulation within the dental biofilm. These include glucosyltransferases, their glucan products, and proteins that bind glucan. At least three glucan binding proteins have been identified, and GbpB, the protein characterized in this study, appears to be novel. The gbpB gene was cloned and the predicted protein sequence contained several unusual features and shared extensive homology with a putative peptidoglycan hydrolase from group B ***streptococcus***. Examination of gbpB genes from clinical isolates of S. mutans revealed that DNA polymorphisms, and hence amino acid changes, were limited to the central region of the gene, suggesting functional conservation within the amino and carboxy termini of the protein. The GbpB produced by clinical isolates and laboratory strains showed various distributions between cells and culture medium, and amounts of protein produced by individual strains correlated positively with their ability to grow as biofilms in an in vitro assay.

L2 ANSWER 5 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

2

AN 2001:397601 BIOSIS

DN PREV200100397601

TI Facilitated intranasal induction of mucosal and systemic immunity to mutans ***streptococcal*** glucosyltransferase peptide vaccines.

AU ***Smith, Daniel J. (1)*** ; King, William F.; Barnes, Leigh A.; Trantolo, Debra; Wise, Donald L.; Taubman, Martin A.

CS (1) Department of Immunology, The Forsyth Institute, 140 The Fenway, Boston, MA, 02115: dsmith@forsyth.org USA

SO Infection and Immunity, (August, 2001) Vol. 69, No. 8, pp. 4767-4773. print.

ISSN: 0019-9567.

DT Article

LA English

SL English

AB Synthetic peptide vaccines which are derived from functional domains of ***Streptococcus*** mutans glucosyltransferases (GTF) have been shown to induce protective immunity in Sprague-Dawley rats after subcutaneous injection in the salivary gland region. Since mucosal induction of salivary immunity would be preferable in humans, we explored methods to induce mucosal antibody in the rat to the GTF peptide vaccines HDS and HDS-GLU after intranasal administration. Several methods of facilitation of the immune response were studied: the incorporation of peptides in bioadhesive poly(D,L-lactide-coglycolide) (PLGA) microparticles, the use of monoepitopic (HDS) or diepitopic (HDS-GLU) peptide constructs, or the use of mucosal adjuvants. Salivary immunoglobulin A (IgA) responses were not detected after intranasal administration of diepitopic HDS-GLU peptide constructs in alum or after incorporation into PLGA microparticles. However, significant primary and secondary salivary IgA and serum IgG antibody responses to HDS were induced in all rats when cholera holotoxin (CT) or a detoxified mutant Escherichia coli heat-labile enterotoxin (R192G LT) were intranasally administered with HDS peptide constructs in PLGA. Coadministration of LT with HDS resulted in predominantly IgG2a responses in the serum, while coadministration with CT resulted in significant IgG1 and IgG2a responses to HDS. Serum IgG antibody, which was induced to the HDS peptide construct by coadministration with these adjuvants, also bound intact mutans ***streptococcal*** GTF in an enzyme-linked immunosorbent assay and inhibited its enzymatic activity. Thus, immune responses which are potentially protective for dental caries can be induced to peptide-based GTF vaccines after mucosal administration if combined with the CT or LT R192G mucosal adjuvant.

L2 ANSWER 6 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

3

AN 2001:337080 BIOSIS

DN PREV200100337080

TI Diepitopic construct of functionally and epitopically complementary peptides enhances immunogenicity, reactivity with glucosyltransferase, and protection from dental caries.

AU Taubman, Martin A. (1); Holmberg, Cynthia J.; ***Smith, Daniel J.***

CS (1) Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA, 02115: mtaubman@forsyth.org USA

SO Infection and Immunity, (July, 2001) Vol. 69, No. 7, pp. 4210-4216. print. ISSN: 0019-9567.

DT Article

LA English

SL English

AB Coimmunization with peptide constructs from catalytic (CAT) and glucan-binding (GLU) domains of glucosyltransferase (GTF) of mutans ***streptococci*** has resulted in enhanced levels of antibody to the CAT construct and to GTF. We designed and synthesized a diepitopic construct (CAT-GLU) containing two copies of both CAT (B epitope only) and GLU (B and T epitope) peptides. The immunogenicity of this diepitopic construct was compared with that of individual CAT and GLU constructs by immunizing groups of Sprague-Dawley rats subcutaneously in the salivary gland vicinity with the CAT-GLU, CAT, or GLU construct or by treating rats by sham immunization. Levels of serum immunoglobulin G (IgG) antibody to

GTF or CAT in the CAT-GLU group were significantly greater than in GLU- or CAT-immunized groups. Immunization with CAT-GLU was compared to coimmunization with a mixture of CAT and GLU in a second rodent experiment under a similar protocol. CAT-GLU immunization resulted in serum IgG and salivary IgA responses to GTF and CAT which were greater than after coimmunization. Immunization with the diepitopic construct and coimmunization with CAT and GLU constructs showed proliferation of T lymphocytes to GTF. Immunization with either the CAT or GLU construct has been shown to elicit significant protection in a rodent dental caries model. Similarly in this study, the enhanced response to GTF after immunization with the CAT-GLU construct resulted in protective effects on dental caries. Therefore, the CAT-GLU diepitopic construct can be a potentially important antigen for a caries vaccine, giving rise to greater immune response than after immunization with CAT, GLU, or a mixture of the two.

L2 ANSWER 7 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

4

AN 2001:303013 BIOSIS

DN PREV200100303013

TI Passive transfer of immunoglobulin Y antibody to ***Streptococcus*** mutans glucan binding protein B can confer protection against experimental dental caries.

AU ***Smith, Daniel J. (1)*** ; King, William F.; Godiska, Ronald

CS (1) Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA, 02115: dsmith@forsyth.org USA

SO Infection and Immunity, (May, 2001) Vol. 69, No. 5, pp. 3135-3142. print. ISSN: 0019-9567.

DT Article

LA English

SL English

AB Active immunization with ***Streptococcus*** mutans glucan binding protein B (GBP-B) has been shown to induce protection against experimental dental caries. This protection presumably results from continuous secretion of salivary antibody to GBP-B, which inhibits accumulation of S. mutans within the oral biofilm. The purpose of this study was to explore the influence of short-term (9- or 24-day) passive oral administration of antibody to S. mutans GBP-B on the longer-term accumulation and cariogenicity of S. mutans in a rat model of dental caries. Preimmune chicken egg yolk immunoglobulin Y (IgY) or IgY antibody to S. mutans GBP-B was supplied in lower (experiment 1) and higher (experiment 2) concentrations in the diet and drinking water of rats for 9 (experiment 1) or 24 (experiment 2) days. During the first 3 days of IgY feeding, all animals were challenged with 5X10⁶ streptomycin-resistant S. mutans strain SJ-r organisms. Rats remained infected with S. mutans for 78 days, during which rat molars were sampled for the accumulation of S. mutans SJ-r bacteria and total ***streptococci***. Geometric mean levels of S. mutans SJ-r accumulation on molar surfaces were significantly lower in antibody-treated rats on days 16 and 78 of experiment 2 and were lower on all but the initial (day 5) swabbing occasions in both experiments. Relative to controls, the extent of molar dental caries measured on day 78 was also significantly decreased. The decrease in molar caries correlated with the amount and duration of antibody administration. This is the first demonstration that passive antibody to S. mutans GBP-B can have a protective effect against cariogenic S. mutans infection and disease.

Furthermore, this decrease in infection and disease did not require continuous antibody administration for the duration of the infection period. This study also indicates that antibody to components putatively involved only in cellular aggregation can have a significant effect on the incorporation of mutans ***streptococci*** in dental biofilm.

L2 ANSWER 8 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

5

AN 2001:384834 BIOSIS

DN PREV200100384834

TI Genotypic diversity of mutans ***streptococci*** in Brazilian nursery children suggests horizontal transmission.

AU Mattos-Graner, Renata O.; Li, Yihong; Caufield, Page W.; Duncan, Margaret; ***Smith, Daniel J. (1)***

CS (1) Department of Immunology, The Forsyth Institute, 140 The Fenway, Boston, MA, 02115: dsmith@forsyth.org USA

SO Journal of Clinical Microbiology, (June, 2001) Vol. 39, No. 6, pp. 2313-2316. print.
ISSN: 0095-1137.

DT Article

LA English

SL English

AB ***Streptococcus*** mutans strains were isolated from cohorts of Brazilian nursery school children and genotyped by arbitrarily primed PCR and restriction fragment length polymorphism analysis. Of 24 children with two to five S. mutans isolates, 29% carried two or more genotypes. The presence of matching genotypes of S. mutans among children attending one nursery suggests horizontal transmission.

L2 ANSWER 9 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

6

AN 2000:222888 BIOSIS

DN PREV200000222888

TI Coimmunization with complementary glucosyltransferase peptides results in enhanced immunogenicity and protection against dental caries.

AU Taubman, Martin A. (1); ***Smith, Daniel J.*** ; Holmberg, Cynthia J.; Eastcott, Jean W.

CS (1) Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA, 02115 USA

SO Infection and Immunity, (May, 2000) Vol. 68, No. 5, pp. 2698-2703.
ISSN: 0019-9567.

DT Article

LA English

SL English

AB Peptide constructs from the catalytic (CAT) and glucan-binding (GLU) regions of the mutans ***streptococcal*** glucosyltransferase enzymes (GTF) can provide immunity to dental caries infection. A strategy of coimmunization was tested to determine whether protection could be enhanced. Rats were immunized with one of the previously described peptide constructs from the CAT or GLU region of the GTF of mutans ***streptococci*** or coimmunized with a combination of these constructs (CAT-GLU). Coimmunized animals demonstrated significantly higher serum immunoglobulin G (IgG) and salivary IgA antibody levels to CAT or GTF than rats immunized with either construct alone. To assess the functional significance of coimmunization with these constructs, animals were

immunized as above or with ***Streptococcus*** sobrinus GTF and then infected with S. sobrinus to explore the effects of immunization on immunological, microbiological, and disease (dental caries) parameters. Serum antibody from the communized group inhibited S. sobrinus GTF-mediated insoluble glucan synthesis in vitro above that of the individual-construct-immunized groups. Immunization with CAT or GLU constructs resulted in significantly reduced dental caries after infection with S. sobrinus compared with sham-immunized animals. Coimmunization produced greater reductions in caries than after immunization with either CAT or GLU. Also, significant elevations in lymphocyte proliferative responses to CAT, GLU, and GTF were observed after coimmunization with CAT-GLU compared with the responses after immunization with the individual constructs. The results suggested that increased numbers of memory T cells, which could proliferate to CAT, were generated by coimmunization. The experiments support the functional significance of these GTF domains in dental caries pathogenesis and present coimmunization as a simple alternative to intact GTF to enhance protective immunity against cariogenic microorganisms.

L2 ANSWER 10 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1999:672601 CAPLUS

DN 131:298658

TI Conjugate vaccines for the prevention of dental caries

IN Lees, Andrew; Taubman, Martin A.; ***Smith, Daniel J.***

PA USA

SO PCT Int. Appl., 54 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952548	A2	19991021	WO 1999-US7828	19990409
WO 9952548	A3	19991202		
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2325338	AA	19991021	CA 1999-2325338	19990409
AU 9934864	A1	19991101	AU 1999-34864	19990409
EP 1069909	A2	20010124	EP 1999-916570	19990409
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1998-81315P P 19980410

WO 1999-US7828 W 19990409

AB The present invention provides glucan-based compns. and methods for stimulating an immune response against mutans ***Streptococci*** components and vaccines and methods for the treatment and prevention of dental caries. In a preferred embodiment, a glucan polymer is covalently bound to one or more T cell-dependent antigens to form a conjugate vaccine. The T cell-dependent antigen preferably contains epitopes of one or more mutans ***streptococcal*** proteins, such as a glucosyltransferase. Moreover, one or more moieties, including haptens, may be conjugated to the glucan or to the glucan-T cell-dependent compn. In a preferred embodiment, these moieties are peptides which contain immunogenic epitopes corresponding to components of a mutants

streptococcus .

L2 ANSWER 11 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

7

AN 2000:63015 BIOSIS

DN PREV200000063015

TI Protective immunity against ***Streptococcus*** mutans infection in mice after intranasal immunization with the glucan-binding region of *S. mutans* glucosyltransferase.

AU Jespersgaard, Christina; Hajishengallis, George; Huang, Yan; Russell, Michael W.; ***Smith, Daniel J.*** ; Michalek, Suzanne M. (1)

CS (1) Department of Microbiology, University of Alabama at Birmingham, 845 South 19th, BBRB 258, Birmingham, AL USA

SO Infection and Immunity, (Dec., 1999) Vol. 67, No. 12, pp. 6543-6549. ISSN: 0019-9567.

DT Article

LA English

SL English

AB Here we present the construction and characterization of a chimeric vaccine protein combining the glucan-binding domain (GLU) of the *gtfB*-encoded water-insoluble glucan-synthesizing glucosyltransferase enzyme (GTF-I) from ***Streptococcus*** mutans and thioredoxin from *Escherichia coli*, which increases the solubility of co-expressed recombinant proteins and stimulates proliferation of murine T cells. The protective potential of intranasal (i.n.) immunization with this chimeric immunogen was compared to that of the GLU polypeptide alone in a mouse infection model. Both immunogens were able to induce statistically significant mucosal (salivary and vaginal) and serum responses ($P < 0.01$) which were sustained to the end of the study (experimental day 100). Following infection with *S. mutans*, sham-immunized mice maintained high levels of this cariogenic organism (approx 60% of the total oral ***streptococci***) for at least 5 weeks. In contrast, animals immunized with the thioredoxin-GLU chimeric protein (Thio-GLU) showed significant reduction (>85%) in *S. mutans* colonization after 3 weeks ($P < 0.05$). The animals immunized with GLU alone required 5 weeks to demonstrate significant reduction (>50%) of *S. mutans* infection ($P < 0.05$). Evaluation of dental caries activity at the end of the study showed that mice immunized with either Thio-GLU or GLU had significantly fewer carious lesions in the buccal enamel or dentinal surfaces than the sham-immunized animals ($P < 0.01$). The protective effects against *S. mutans* colonization and caries activity following i.n. immunization with GLU or Thio-GLU are attributed to the induced salivary immunoglobulin A (IgA) anti-GLU responses. Although in general Thio-GLU was not significantly better than GLU alone in stimulating salivary IgA responses and in protection against dental caries, the finding that the GLU polypeptide alone, in the absence of any immunoenhancing agents, is protective against disease offers a promising and safe strategy for the development of a vaccine against caries.

L2 ANSWER 12 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

8

AN 1999:262698 BIOSIS

DN PREV199900262698

TI Antibody to glucosyltransferase induced by synthetic peptides associated with catalytic regions of alpha-amylases.

AU ***Smith, Daniel J. (1)*** ; Heschel, Rhonda L.; King, William F.;
Taubman, Martin A.
CS (1) Department of Immunology, Forsyth Dental Center, 140 The Fenway,
Boston, MA, 02115 USA
SO Infection and Immunity, (May, 1999) Vol. 67, No. 5, pp. 2638-2642.
ISSN: 0019-9567.
DT Article
LA English
SL English
AB We examined the immunogenicity and induction of inhibitory activity of
19-mer synthetic peptides which contained putative catalytic regions that
were associated with the beta5 (EAW) and beta7 (HDS) strand elements of
the suggested (beta, alpha)8 catalytic barrel domain of
Streptococcus mutans glucosyltransferase (GTF). Both peptides
readily induced serum immunoglobulin G (IgG) and salivary IgA antipeptide
activity which was reactive both with the inciting peptide and with intact
S. mutans GTF. Antisera to each peptide construct also inhibited the
ability of S. mutans GTF to synthesize glucan. These observations support
the existence of catalytic subdomains containing glutamate and tryptophan
(EAW) or aspartate and histidine (HDS) residues, each of which have been
suggested to be involved with the catalytic activity of GTF. Furthermore,
the epitopes defined in these sequences have significant immunogenicity
and can induce immune responses which interfere with GTF-mediated glucan
synthesis.

L2 ANSWER 13 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
9

AN 1999:111341 BIOSIS
DN PREV199900111341
TI Functional and immunogenic characterization of two cloned regions of
Streptococcus mutans glucosyltransferase I.
AU Jespergaard, Christina; Hajishengallis, George; Greenway, Terrence E.;
Smith, Daniel J. ; Russell, Michael W.; Michalek, Suzanne M. (1)
CS (1) Dep. Microbiol., Univ. Ala., 845 S. 19th, BBRB 258, Birmingham, AL
35294-2170 USA
SO Infection and Immunity, (Feb., 1999) Vol. 67, No. 2, pp. 810-816.
ISSN: 0019-9567.
DT Article
LA English
AB Glucosyltransferase (GTF) enzymes of mutans ***streptococci*** are
considered virulence factors due to their ability to synthesize adhesive
glucans, which facilitate cell-to-cell adherence and accumulation. In this
study we report the cloning, expression, and characterization of the
catalytic (CAT) and glucan-binding (GLU) domains of S. mutans GTF-I
encoded by gtfB. The CAT and GLU polypeptides represent amino acid
residues 253 to 628 and 1183 to 1473, respectively, of S. mutans GTF-I.
Antibodies to recombinant CAT and GLU were generated in rabbits and
purified by affinity chromatography. Purified anti-CAT antibodies
significantly inhibited water-insoluble glucan synthesis by S. mutans and
S. sobrinus GTFs ($P < 0.0001$ and $P < 0.05$, respectively). The purified
anti-GLU antibodies significantly inhibited both water-insoluble and
water-soluble glucan synthesis by S. mutans GTFs ($P < 0.0001$ and $P < 0.05$,
respectively). These results demonstrate that anti-CAT and anti-GLU
antibodies are capable of inhibiting a variety of GTF activities. Since
antibodies to S. mutans in saliva are implicated in protection against

disease, we next assessed the ability of CAT and GLU polypeptides to induce mucosal antibody responses in mice. Intranasal (i.n.) immunization of mice with CAT showed significantly ($P < 0.005$) elevated levels of specific immunoglobulin G (IgG) antibody activity in serum and specific IgA antibody activity in serum, saliva, vaginal washes, and fecal samples. GLU immunized animals showed significantly ($P < 0.005$) elevated levels of specific IgA antibody activity in serum and vaginal secretions. Taken together, these results demonstrate that the recombinant CAT and GLU polypeptides are effective in inducing both mucosal and systemic immune responses. The ability of these polypeptides to induce a mucosal IgA immune response in mice after i.n. immunization supports their use as subunit vaccine candidates in the development of an anticaries vaccine.

L2 ANSWER 14 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
10

AN 1998:505575 BIOSIS

DN PREV199800505575

TI Structural and antigenic characteristics of ***Streptococcus***
sobrinus glucan binding proteins.

AU ***Smith, Daniel J. (1)*** ; King, William F.; Wu, Christine D.; Shen,
Bella I.; Taubman, Martin A.

CS (1) Dep. Immunol., Forsyth Dent. Cent., 140 The Fenway, Boston, MA 02115
USA

SO Infection and Immunity, (Nov., 1998) Vol. 66, No. 11, pp. 5565-5569.
ISSN: 0019-9567.

DT Article

LA English

AB Three purified glucan binding proteins (GBP-2, GBP-3, and GBP-5) from
Streptococcus sobrinus 6715 were compared structurally by mass
spectroscopy of tryptic fragments and antigenically by Western blot
analysis with rat antisera to each GBP or to peptides containing putative
glucan binding epitopes of mutans ***streptococcal***
glucosyltransferases. Structural and antigenic analyses indicated that
GBP-3 and GBP-5 are very similar but that both are essentially unrelated
to GBP-2. None of these *S. sobrinus* GBPs appeared to have a strong
antigenic relationship with GBPs from ***Streptococcus*** mutans.
Thus, *S. sobrinus* GBP-2 and GBP-3 appear to be distinct proteins with
potentially different functions. *S. sobrinus* GBP-5 may be a proteolytic
fragment of GBP3, or, alternatively, the genes coding for these proteins
may be closely related.

L2 ANSWER 15 OF 45 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 11

AN 1997:735840 CAPLUS

DN 128:21853

TI Synthetic peptide vaccines for dental caries

IN Taubman, Martin A.; ***Smith, Daniel J.***

PA Forsyth Dental Infirmary for Children, USA

SO U.S., 11 pp. Cont.-in-part of U.S. Ser. No. 877,295, abandoned.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI US 5686075	A	19971111	US 1993-57162	19930430
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US 2001048926 A1 20011206 US 1997-967573 19971110
PRAI US 1992-877295 B2 19920501
US 1993-57162 A2 19930430

AB Immunization of animals with a compn. contg. either an amino acid sequence from the catalytic domain of glucosyltransferase, an amino acid sequence from the glucan-binding region of glucosyltransferase or an amino acid sequence from the native surface domain of glucosyltransferase provoke antibody and T-cell immune responses to this enzyme. Since this enzyme has been implicated in the colonization of mutans ***streptococci*** on tooth surfaces, such immune responses are important for the prevention of dental caries. Multicomponent and multivalent compns. which include these amino acid sequences provide effective vaccine capabilities.

L2 ANSWER 16 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
12

AN 1997:515418 BIOSIS

DN PREV199799814621

TI Immunogenicity and protective immunity induced by synthetic peptides associated with a catalytic subdomain of mutans group ***streptococcal*** glucosyltransferase.

AU ***Smith, Daniel J. (1)*** ; Shoushtari, Babak; Heschel, Rhonda L.; King, William F.; Taubman, Martin A.

CS (1) Dep. Immunol., Forsyth Dent. Cent., 140 Fenway, Boston, MA 02115 USA

SO Infection and Immunity, (1997) Vol. 65, No. 11, pp. 4424-4430.

ISSN: 0019-9567.

DT Article

LA English

AB We examined the immunogenicity and induction of protective immunity of two 19-mer sequences (GGY and AND) which overlapped a highly conserved region which has recently been implicated in the enzymatic activity of glucosyltransferases (GTFs) of the mutans group ***streptococci***. These peptides were synthesized as eight-branched constructs on a lysine core. Serum immunoglobulin G (IgG) antibody, induced by subcutaneous (s.c. (salivary gland vicinity)) injection with these peptide constructs, reacted with the inciting antigen, with mutans ***streptococcal*** GTFs, and with a 21-mer peptide (CAT) containing an aspartate previously shown to covalently bind sucrose. Several of these antisera also inhibited the ability of ***Streptococcus*** sobrinus GTF to synthesize insoluble glucan. Significant levels of salivary IgA antibody were also induced by GGY and AND peptide constructs after s.c. injection. The effect of immunization with the GGY and AND peptide constructs on the cariogenicity of ***Streptococcus*** mutans was studied in three experiments by immunization of weanling Sprague-Dawley rats, twice at 7- to 14-day intervals with peptides, S. sobrinus GTF, or phosphate-buffered saline. All rats were then orally infected with S. mutans SJ. After 63-day infection periods, the GGY and AND-injected groups had significant dental caries reductions compared with sham-injected groups in most experiments. These studies support the existence of an additional catalytic subdomain within the sequence defined by the GGY and AND peptides. Furthermore, the epitopes defined in these sequences have significant immunogenicity, can induce immune responses which interfere with GTF-mediated glucan synthesis in vitro, and can protect rats from experimental dental caries.

L2 ANSWER 17 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
13

AN 1996:438622 BIOSIS
DN PREV199699152228
TI Experimental immunization of rats with a ***Streptococcus*** mutans
59-kilodalton glucan-binding protein protects against dental caries.
AU ***Smith, Daniel J. (1)*** ; Taubman, Martin A.
CS (1) Dep. Immunol., Forsyth Dent. Cent., Boston, MA 02115 USA
SO Infection and Immunity, (1996) Vol. 64, No. 8, pp. 3069-3073.
ISSN: 0019-9567.
DT Article
LA English
AB Glucan-binding proteins (GBPs) are theoretically important in the
molecular pathogenesis of dental caries caused by ***Streptococcus***
mutans. The present study evaluated the ability of antibody induced by the
S. mutans 59-kDa GBP (GBP-59) to affect dental caries caused by
experimental infection with S. mutans in a rodent model. Groups of
20-day-old rats were injected twice at 9-day intervals subcutaneously in
the salivary gland vicinity with GBP-59, glucosyltransferase (GTF), or
phosphate-buffered saline (sham injection), each incorporated in an
adjuvant. Two weeks after the second injection, GBP-59- and GTF-injected
rats contained significant levels of salivary immunoglobulin A and serum
immunoglobulin G antibody to the respective injected antigens. However,
cross-reacting antibody to S. mutans GTF or GBP-59 was not induced by the
respective antigen. Rats were then orally infected with S. mutans. After
71 days of infection, GBP-59- and GTF-injected groups had smaller numbers
of S. mutans on their molar surfaces, compared with the sham-injected
infected group. Total, sulcal, and smooth-surface molar caries in the
GBP-59- and GTF-immunized S. mutans-infected groups were each
significantly lower (P < 0.003) than the respective measures of
caries in the sham injected infected group. The results of this
investigation demonstrate that immunization with S. mutans GBP-59 induces
an immune response in rats that can interfere with the accumulation of S.
mutans and can reduce the level of dental caries caused by this cariogenic
streptococcus. Furthermore, the protective immunity induced by
either GBP-59 or GTF appears to result from antibodies to independent
epitopes since these two S. mutans components do not have a close
antigenic relationship.

L2 ANSWER 18 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
14

AN 1995:409470 BIOSIS
DN PREV199598423770
TI Immunization of rats with synthetic peptide constructs from the
glucan-binding or catalytic region of mutans ***streptococcal***
glucosyltransferase protects against dental caries.
AU Taubman, Martin A. (1); Holmberg, Cynthia J.; ***Smith, Daniel J.***
CS (1) Dep. Immunol., Forsyth Dental Center, Boston, MA 02115 USA
SO Infection and Immunity, (1995) Vol. 63, No. 8, pp. 3088-3093.
ISSN: 0019-9567.
DT Article
LA English
AB Previously, we have described peptide constructs from two regions of
glucosyltransferase (GTF) of mutans ***streptococci***. A putative
catalytic site in the amino-terminal half of the molecule and a repeated
glucan-binding site in the carboxyl-terminal half of GTF were the regions
upon which sequences were based. The present study explored the effects of

immunization with these peptide constructs (called CAT or GLU) and with ***streptococcal*** GTFs from ***Streptococcus*** sobrinus and S. mutans on immunological, microbiological, and disease parameters. Groups of immunized Sprague-Dawley rats were infected with either 10-8 S. sobrinus 6715 or 10-8 S. mutans SJ32 organisms. Serum immunoglobulin G antibody levels, determined by enzyme-linked immunosorbent assay, to the respective peptide constructs and to the appropriate ***streptococcal*** GTF were significantly increased (after immunization) prior to infection and at the end of the experiment. Also, serum antibody from CAT-, GLU-, and S. sobrinus GTF-immunized rats inhibited S. sobrinus GTF-mediated insoluble glucan synthesis (all) and S. mutans GTF-mediated soluble glucan synthesis (all except anti-GLU) from sucrose. Immunization with the CAT or GLU peptide construct resulted in significantly reduced smooth surface and sulcal caries after infection with S. sobrinus. Sulcal dental caries after infection with S. mutans SJ32 were also significantly reduced in CAT- and GLU-immunized rats. Thus, immunization with peptides whose sequences are based on putative functional domains of mutans ***streptococcal*** GTF are protective toward a cariogenic S. sobrinus or S. mutans infection.

L2 ANSWER 19 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1995:970032 CAPLUS

DN 124:84183

TI Potential for glucosyltransferase-based synthetic peptides in a dental caries vaccine

AU ***Smith, Daniel J.*** ; Taubman, Martin A.

CS Department of Immunology, Forsyth Dental Center, Boston, MA, 02115, USA

SO Adv. Exp. Med. Biol. (1995), Volume Date 1995, 371B, 1157-9

CODEN: AEMBAP; ISSN: 0065-2598

DT Journal

LA English

AB The antigenicity and immunogenicity of MAP constructs contg. 4 copies of peptides derived from sequences assocd. with the glucan-binding or catalytic domains of glucosyltransferase were studied in humans and rats. Both constructs reacted with several human serum IgG and salivary IgA antibody samples, and were immunogenic in rats, giving rise to high levels of anti-peptide serum IgG. These results are discussed in the context of developing a vaccine for dental caries.

L2 ANSWER 20 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1995:970029 CAPLUS

DN 124:53208

TI Development of salivary IgA antibody to oral ***streptococcal*** antigens associated with virulence

AU ***Smith, Daniel J.*** ; Taubman, Martin A.

CS Department of Immunology, Forsyth Dental Center, Boston, MA, 02115, USA

SO Adv. Exp. Med. Biol. (1995), Volume Date 1995, 371B, 1141-3

CODEN: AEMBAP; ISSN: 0065-2598

DT Journal

LA English

AB The authors studied the relationship between the initial infection with ***Streptococcus*** mutans and the appearance of the salivary antibody to ***streptococcal*** antigens that may be involved in colonization (glucosyltransferase, glucan-binding protein, and antigen I/II).

L2 ANSWER 21 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

AN 1995:39909 BIOSIS

DN PREV199598054209

TI Immunological Characteristics of a Synthetic Peptide Associated with a Catalytic Domain of Mutans ***Streptococcal*** Glucosyltransferase.

AU ***Smith, Daniel J. (1)*** ; Taubman, Martin A.; King, William F.; Eida, Stephen; Powell, Jonathan R.; Eastcott, Jean

CS (1) Dep. Immunol., Forsyth Dent. Cent., Boston, MA 02115 USA

SO Infection and Immunity, (1994) Vol. 62, No. 12, pp. 5470-5476.

ISSN: 0019-9567.

DT Article

LA English

AB The immunogenicity of a multiple antigenic peptide construct consisting of four copies of the synthetic 21-mer peptide DANFDSIRVDAVDNVDADLLQ was measured. The composition of this peptide was derived from a sequence in the N-terminal region of mutans ***streptococcal*** glucosyltransferases (GTFs) containing an aspartic acid implicated in catalysis. The peptide (CAT) construct was synthesized as a tetramer on a lysine backbone and subcutaneously injected into Sprague-Dawley rats for polyclonal antibody formation or intraperitoneally injected into BALB/c mice, and then spleen cell fused with Sp2/OAg14 murine myeloma cells for monoclonal antibody formation. The resulting rat antisera and mouse monoclonal antibodies reacted with CAT and with native GTF isozymes from ***Streptococcus*** sobrinus and ***Streptococcus*** mutans (in enzyme-linked immunosorbent assay and Western blot (immunoblot) analyses). Functional inhibition of the water-insoluble glucan synthetic activity of *S. sobrinus* GTF-I was demonstrated with an immunoglobulin M anti-CAT monoclonal antibody (gt 80% inhibited) and with rat sera (approximately 17% inhibited). The monoclonal antibody preparation also modestly inhibited the water-soluble glucan synthetic activity of an *S. mutans* GTF mixture. These results suggest that the CAT peptide contains B-cell epitopes that are similar to those of intact mutans ***streptococcal*** GTFs and has the potential to elicit antibody that can inhibit GTF function. Thus, sequences within this peptide construct may have value for inclusion in a synthetic dental caries vaccine.

L2 ANSWER 22 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

AN 1994:301149 BIOSIS

DN PREV199497314149

TI Purification and antigenicity of a novel glucan-binding protein of ***Streptococcus*** mutans.

AU ***Smith, Daniel J. (1)*** ; Akita, Hirotoshi; King, William F.; Taubman, Martin A.

CS (1) Dep. Immunol., Forsyth Dental Cent., 140 The Fenway, Boston, MA 02115 USA

SO Infection and Immunity, (1994) Vol. 62, No. 6, pp. 2545-2552.

ISSN: 0019-9567.

DT Article

LA English

AB A novel glucan-binding protein (GBP) having an apparent molecular mass of 59 kDa (GBP-59) has been purified from ***Streptococcus*** mutans SJ by a combination of affinity chromatography on alpha-1,6-linked glucan, gel filtration chromatography, and ion-exchange chromatography. GBP-59 was distinct from the quantitatively predominant *S. mutans* GBP (GBP-74) on the

basis of size, elution position in a salt gradient, and antigenicity. Rat antisera to purified GBP-59 and GBP-74 did not cross-react. GBP-59 is apparently immunogenic in humans, since immunoglobulin A (IgA) antibody in 20 of 24 adult parotid saliva samples was shown to react with GBP-59 in an enzyme-linked immunosorbent assay. The glucan-binding activity of GBP-59 was confirmed by anti-GBP-59 immunogold labelling of Sephadex G-50 that had been preincubated with *S. mutans* culture supernatant. GBP-59 could be detected in culture supernatants of all laboratory strains of *S. mutans* (e.g., Ingbritt), as well as all strains of *S. mutans* that had been recently isolated from young children. GBP-59 was often the only component in protease inhibitor-containing 4-h *S. mutans* culture supernatants that reacted with human parotid salivary IgA antibody in Western blot (immunoblot) analyses. These studies suggest that GBP-59 is a structurally and antigenically distinct *S. mutans* GBP that can elicit significant levels of salivary IgA antibody in humans.

L2 ANSWER 23 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1994:86402 CAPLUS

DN 120:86402

TI Synthetic peptide vaccines for dental caries

IN Taubman, Martin A.; ***Smith, Daniel J.***

PA Forsyth Dental Infirmary for Children, USA

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9322341	A1	19931111	WO 1993-US4094	19930430
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 638092	A1	19950215	EP 1993-910953	19930430
R: BE, CH, DE, DK, FR, GB, IE, IT, LI, NL, SE				
JP 07506374	T2	19950713	JP 1993-519549	19930430
PRAI US 1992-877295	A	19920501		
WO 1993-US4094	W	19930430		

AB Immunization of animals with a compn. contg. either an amino acid sequence from the catalytic domain, glucan-binding region, and native surface domain of glucosyltransferase (I) provoke antibody and T-cell immune responses to this enzyme. Since this enzyme has been implicated in the colonization of mutans ***streptococci*** on tooth surfaces, such immune responses are important for the prevention of dental caries. Sequences of synthetic I-derived peptides are included. The immunogenicity of the synthetic peptides was detd. in rats, as was reactivity of T and B lymphocytes to I in human.

L2 ANSWER 24 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

17

AN 1993:410070 BIOSIS

DN PREV199396075795

TI Antigenicity and immunogenicity of a synthetic peptide derived from a glucan-binding domain of mutans ***streptococcal*** glucosyltransferase.

AU ***Smith, Daniel J. (1)*** ; Taubman, Martin A.; Holmberg, Cynthia F.;

Eastcott, Jean; King, William F.; Ali-Salaam, Pia
CS (1) Dep. Immunol., Forsyth Dent. Cent., Boston, MA 02115 USA
SO Infection and Immunity, (1993) Vol. 61, No. 7, pp. 2899-2905.
ISSN: 0019-9567.

DT Article

LA English

AB The immunogenicity and antigenicity of a multiply antigenic peptide construct containing four copies of the synthetic peptide TGAQTIKGQKLYFKANGQQVKG were measured in rodents and humans, respectively. The composition of this peptide construct (termed GLU) was derived from a major repeating sequence in the C-terminal region of mutans ***streptococcal*** glucosyltransferases that synthesize water-insoluble glucan (GTF-I). The GLU peptide elicited high levels of serum immunoglobulin G antibody to GLU after subcutaneous injection into Sprague-Dawley rats. These antisera also reacted with intact GTF isozymes from ***Streptococcus*** sobrinus and ***Streptococcus*** mutans (by enzyme-linked immunosorbent assay (ELISA) and Western blot (immunoblot) analyses) and with an 87-kDa glucan-binding protein from S. sobrinus (by Western blot). The synthesis of filter-retained glucan by GTF-Sd of S. sobrinus could be inhibited (30%) by preincubation with anti-GLU rat serum. Splenic and lymph node lymphocytes from rats injected once with S. sobrinus GTF isozymes demonstrated significant proliferation after 5 days of culture with GLU. The GLU peptide reacted with 4 of 29 human parotid saliva samples and 5 of 29 human serum samples (by ELISA). These results suggest that the GLU peptide contains B- and T-cell epitopes that are similar to those of intact mutans ***streptococcal*** GTFs and possibly certain other glucan-binding proteins as well. Furthermore, since antibody to this epitope(s) appears to inhibit GTF function, sequences within this peptide construct may have value for inclusion in a synthetic dental caries vaccine.

L2 ANSWER 25 OF 45 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1993:470749 BIOSIS

DN PREV199345093874

TI Emergence of immune competence in saliva.

AU ***Smith, Daniel J. (1)*** ; Taubman, Martin A.

CS (1) Dep. Immunol., Forsyth Dental Cent., Boston, MA 02115 USA

SO Critical Reviews in Oral Biology & Medicine, (1993) Vol. 4, No. 3-4, pp. 335-341.

Meeting Info.: Symposium on Contemporary Developments in Salivary Research

Buffalo, New York, USA November 6-10, 1991

ISSN: 1045-4411.

DT Article

LA English

L2 ANSWER 26 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1986:495855 CAPLUS

DN 105:95855

TI Caries immunity and immune responses to ***Streptococcus*** mutans glucosyltransferase

AU Taubman, Martin A.; ***Smith, Daniel J.*** ; Ebersole, Jeffrey L.; Stack, Wendy E.; Tsukuda, Tomio; Trocme, Marie C.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, MA, 02115, USA

SO Mol. Microbiol. Immunobiol. Streptococcus Mutans, Proc. Int. Conf. "Cell., Mol. Clin. Aspects Streptococcus Mutans" (1986), Meeting Date 1985,

279-86. Editor(s): Hamada, Shigeyuki. Publisher: Elsevier, Amsterdam, Neth.

CODEN: 55CZAF

DT Conference

LA English

AB Extirpation of Peyer's patches and/or mesenteric lymph nodes dramatically decreased the serum IgA response to *S. mutans* glucosyltransferase (GTF) in rats. Also, neonatally thymectomized or congenitally athymic rats produced little or no salivary antibody response to GTF. Athymic animals were more susceptible to dental caries than normal controls; however, immunization with anti-GTF antibodies reduced susceptibility to caries in both groups.

L2 ANSWER 27 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1985:539981 CAPLUS

DN 103:139981

TI Salivary IgA antibody to glucosyltransferase in man

AU ***Smith, Daniel J.*** ; Taubman, M. A.; Ebersole, J. L.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, MA, 02115, USA

SO Clin. Exp. Immunol. (1985), 61(2), 416-24

CODEN: CEXIAL; ISSN: 0009-9104

DT Journal

LA English

AB Parotid salivas of 97 young adults were screened for IgA antibody to glucosyltransferase (GTF) from lab. strains of ***Streptococcus*** mutans (serotypes c and g). Antibody levels to GTF from serotype c pos. correlated with levels to serotype-g GTF among these salivas. GTFs were prep'd. from *S. mutans* obtained from a subset of individuals in this population. All but 1 saliva showed IgA antibody activity to all of the GTF tested. In addn., the relative magnitude of each subject's antibody level was generally the highest to the GTF from his own *S. mutans*. Fractions enriched for IgA by (NH₄)₂SO₄ pptn. and gel filtration showed patterns of functional inhibition of GTF activity which were consistent with patterns of IgA antibody activity in ELISA of unfractionated salivas. These data indicate that (1) detectable levels of IgA antibody to *S. mutans* GTF exist in many young adult salivas, (2) while this IgA antibody activity reacts with GTF from different biotypes, subjects generally show the highest secretory IgA antibody levels to their own GTF, and (3) the relative amt. of IgA antibody to GTF and the ability to inhibit GTF activity are roughly correlated.

L2 ANSWER 28 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1984:435199 CAPLUS

DN 101:35199

TI Glucosyltransferase

IN Taubman, Martin A.; ***Smith, Daniel J.***

PA Forsyth Dental Infirmary for Children, USA

SO PCT Int. Appl., 12 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 8401170	A1	19840329	WO 1983-US1359	19830909
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W: JP, US

RW: AT, BE, CH, DE, FR, GB, LU, NL, SE

US 4438200 A 19840320 US 1982-416869 19820913
CA 1183477 A1 19850305 CA 1983-420426 19830128
EP 118547 A1 19840919 EP 1983-903053 19830909
EP 118547 B1 19910116

R: AT, BE, CH, DE, FR, GB, LI, NL, SE

JP 59501696 T2 19841011 JP 1983-503130 19830909
JP 04040989 B4 19920706
AT 60086 E 19910215 AT 1983-903053 19830909

PRAI US 1982-416869 19820913

EP 1983-903053 19830909

WO 1983-US1359 19830909

AB Glucosyltransferase (I) useful for immunization against dental caries is prepd. by culturing ***Streptococcus*** mutans in a medium contg. glucose and dialyzable nutrients and recovering I from the supernatant of the cultured cells by using a H₂O-insol. polyglucan matrix. I is concd. and purified by Sepharose CL-4B gel filtration using 6M guanidine-HCl for elution. Thus, I is prepd. from the supernatant of S. mutans cultures by admixing the supernatant with H₂O-insol. Sephadex beads prepd. by crosslinking dextrans of Leuconostoc mesenteroides with epichlorohydrin. After recovery and washing, the I-Sephadex bead complex is treated with a denaturing solvent (6M guanidine-HCl for 2 h at 37.degree.) to disrupt the complex and provide a I-denaturing solvent mixt.

L2 ANSWER 29 OF 45 USPATFULL

AN 84:15901 USPATFULL

TI Method for the preparation of glucosyltransferase

IN Taubman, Martin A., Newton, MA, United States

Smith, Daniel J., Natick, MA, United States

PA Forsyth Dental Infirmary for Children, Boston, MA, United States (U.S. corporation)

PI US 4438200 19840320

AI US 1982-416869 19820913 (6)

DT Utility

FS Granted

EXNAM Primary Examiner: Shapiro, Lionel M.

LREP Crowley, Richard P.

CLMN Number of Claims: 14

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 284

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of preparing a purified glucosyltransferase (GTF) for use in immunization against dental caries, which method comprises: culturing a ***Streptococcus*** mutans in a medium containing glucose and dialyzable nutrients to form a mixture of culture cells and supernatant; recovering the supernatant by the removal of the culture cells; admixing the recovered supernatant with a water-insoluble, polymerized polysaccharide as solid particulate material for a period of time, to provide a GTF, solid particulate complex; recovering the GTF complex in solid particulate form by filtration; washing the solid GTF complex to remove unbound GTF and medium components; removing GTF from the solid particulate material by a denaturing solvent; recovering the water-insoluble particulate material for reuse in the method; and

recovering the GTF from the water-insoluble polysaccharide and purifying the recovered GTF.

L2 ANSWER 30 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1983:468750 CAPLUS

DN 99:68750

TI Adjuvants for secretory immune responses

AU Taubman, Marin A.; Ebersole, Jeffrey L.; ***Smith, Daniel J.*** ;
Stack, Wendy

CS Dep. Immunol., Forsyth Dent. Cent., Boston, MA, 02115, USA

SO Ann. N. Y. Acad. Sci. (1983), 409(Secretory Immune Syst.), 637-49

CODEN: ANYAA9; ISSN: 0077-8923

DT Journal

LA English

AB Salivary IgA responses of rats receiving synthetic muramyl dipeptide (MDP) were elevated after oral glucosyltransferase (GTF) antigen administration and after infection with ***Streptococcus*** mutans bearing surface GTF. Intragastric (i.g.) administration (but not injection) of MDP enhanced salivary IgA responses to i.g. GTF. S.c. injection (but not i.g. administration) of MDP enhanced IgA responses to GTF injected in the vicinity of the salivary gland. Conjugation of MDP to GTF did not enhance the secretory response to the antigen. Nevertheless salivary gland vicinity administration of ovalbumin in incomplete Freund's adjuvant dramatically enhanced the secretory and serum responses. Injection of MDP may further enhance the secretory response. The combination of routes of adjuvant and antigen administration were crit. in selectively enhancing a secretory immune response.

L2 ANSWER 31 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1984:470647 CAPLUS

DN 101:70647

TI Protective aspects of immune response to glucosyltransferase in relation to dental caries

AU Taubman, Martin A.; ***Smith, Daniel J.*** ; Ebersole, Jeffrey L.;
Hillman, Jeffrey D.

CS Dep. Immunol., Forsyth. Dent. Cent., Boston, MA, 02115, USA

SO Glucosyltransferases, Glucans, Sucrose Dent. Caries, [Workshop] (1983),
Meeting Date 1982, 249-58. Editor(s): Doyle, R. J.; Ciardi, J. E.

Publisher: IRL, Washington, D. C.

CODEN: 51ZJAK

DT Conference

LA English

AB Antibody to glucosyltransferase (GTF) can interfere with ***Streptococcus*** mutans accumulation in dental plaques both in vitro and in vivo. The redns. in caries subsequent to the interference with accumulation can be correlated with salivary IgA antibody. The redns. in caries or lesions extend beyond serotype boundaries. Studies of antibody to GTF in vitro provided extensive evidence demonstrating the mode of this antibody function in vivo. Antibody to S. mutans enhanced the permeability of plaque such that either diffusion of acid away from the surface and/or diffusion of buffer ions toward the surface was facilitated. Further studies with antibody to GTF-I indicated the water-insol. polyglucans (WIP) synthesized by GTF were preferentially inhibited and that water-sol.-polyglucans were not inhibited. Thus, immunol. interference with dental caries caused by S. mutans can now be

explained on the mol. level. Antibody to GTF interferes with bacterial accumulation, and preferentially inhibits WIP synthesis. This inhibition results in a more porous plaque. Thus, the reduced levels of caries seen in immunized rodents could be the result of fewer bacteria secreting acid in a more porous plaque.

L2 ANSWER 32 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1984:470646 CAPLUS

DN 101:70646

TI Adjuvants, glucosyltransferase and caries vaccine

AU Ebersole, Jeffrey L.; Taubman, Martin A.; ***Smith, Daniel J.***

CS Dep. Immunol., Forsyth Dent. Cent., Boston, MA, 02115, USA

SO Glucosyltransferases, Glucans, Sucrose Dent. Caries, [Workshop] (1983), Meeting Date 1982, 241-8. Editor(s): Doyle, R. J.; Ciardi, J. E.

Publisher: IRL, Washington, D. C.

CODEN: 51ZJAK

DT Conference

LA English

AB Regulation of salivary IgA (SIgA) responses to glucosyltransferase (GTF) from ***Streptococcus*** mutans was examd. in the rat. T-cell depletion of rat via neonatal thymectomy (Tx) resulted in a lack of ability to respond to GTF in soln. with SIgA antibodies. Likewise, the Tx rats exhibited a significantly decreased response to GTF when presented on the surface of S. mutans. Further studies indicated that particulate GTF antigen bound to its product (water-insol. polysaccharide) was more efficient at eliciting SIgA antibodies than sol. antigen. Studies of the effect of adjuvants on the SIgA antibody response showed that Al(OH)₃, complete Freund's adjuvant, and muramyl dipeptide enhanced SIgA antibody prodn. when injected locally or administered intragastrically.

L2 ANSWER 33 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1984:470645 CAPLUS

DN 101:70645

TI Antigenic relatedness of glucosyltransferases from ***Streptococcus*** mutans and ***Streptococcus*** sanguis

AU ***Smith, Daniel J.*** ; Taubman, Martin A.; Ebersole, Jeffrey L.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, MA, 02115, USA

SO Glucosyltransferases, Glucans, Sucrose Dent. Caries, [Workshop] (1983), Meeting Date 1982, 223-30. Editor(s): Doyle, R. J.; Ciardi, J. E.

Publisher: IRL, Washington, D. C.

CODEN: 51ZJAK

DT Conference

LA English

AB The antigenic relationships among glucosyltransferases (GTF) from S. mutans were investigated using techniques measuring the binding of antibody to radiolabeled GTF or to GTF attached to polystyrene, or measuring the ability of antibody to inhibit GTF activity. IgG antibody to GTF from serotype c or g strains of S. mutans could bind to or inhibit the activity of GTF from homologous serotypes. However, IgG antibody to GTF from the g serotype reacted more strongly with GTF from serotypes a, d, and g than from serotypes c and e. Conversely, IgG antibody to GTF from the c serotype reacted best with GTF from serotypes c and e. Measurement of antibody activity in saliva generally revealed the same relationships. However, broad cross-protection was obsd. when these relationships were explored in vivo. The in vitro binding of IgG antibody

to S. mutans GTF was low but significant for GTF from S. sanguis strains 10558, H7PR3, and 34. IN vivo, significantly fewer rodents immunized with S. mutans GTF and subsequently challenged with S. sanguis H7PR3 remained infected compared with sham-immunized and challenged control groups. However, immunization with GTF from S. sanguis 34 did not influence the course of infection or disease after infection with cariogenic S. mutans.

L2 ANSWER 34 OF 45 USPATFULL

AN 81:8080 USPATFULL

TI Method of preparing a purified glucosyltransferase

IN Taubman, Martin A., Newton, MA, United States

Smith, Daniel J., Natick, MA, United States

PA Forsyth Dental Infirmary for Children, Boston, MA, United States (U.S. corporation)

PI US 4250262 19810210

AI US 1979-103590 19791214 (6)

RLI Continuation of Ser. No. US 1978-956847, filed on 2 Nov 1978, now abandoned which is a division of Ser. No. US 1978-879432, filed on 21 Feb 1978, now patented, Pat. No. US 4150116, issued on 17 Apr 1979

DT Utility

FS Granted

EXNAM Primary Examiner: Shapiro, Lionel M.

LREP Crowley, Richard P.

CLMN Number of Claims: 13

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1795

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Immunization of animals with preparations containing more purified forms of glucosyltransferase (GTF) results in the presence of antibody in saliva demonstrable by functional inhibitions of enzyme activity and binding of radioactive enzyme. Serum antibody was also present. Immunized groups of animals had lower mean caries scores than comparably sham-immunized or nonimmunized control groups. Local immunization with GTF of serotype c or g of a ***Streptococcus*** mutans reduces the colonization, caries, and lesions caused by infection with S. mutans of serotype g (strain 6715) or c, or with serotype g or c, or with serotype a or g, respectively.

L2 ANSWER 35 OF 45 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 18

AN 1979:454528 CAPLUS

DN 91:54528

TI Immunization against dental caries with glucosyltransferase antigens

IN Taubman, Martin A.; ***Smith, Daniel J.***

PA Forsyth Dental Infirmary for Children, USA

SO U.S., 18 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 4150116	A	19790417	US 1978-879432	19780221
CA 1152000	A1	19830816	CA 1979-322048	19790221
US 4250262	A	19810210	US 1979-103590	19791214

PRAI US 1978-879432 19780221

US 1978-956847 19781102

AB Immunization of animals with preps. contg. bacterial glucosyltransferase resulted in the presence of antibody in saliva demonstrable by functional inhibition of enzyme activity and binding of radioactive enzyme. Serum antibody was also present. Immunized groups of animals had lower mean caries scores than comparably sham-immunized or nonimmunized control groups. Local immunization with glucosyltransferase of serotype c or g of a ***Streptococcus*** mutans reduced the colonization, caries, and lesions caused by infection with S. mutans of serotype g (strain 6715) or c, or with serotype g or c, or with serotype a or g, resp.

L2 ANSWER 36 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1979:163806 CAPLUS

DN 90:163806

TI Preparation of glucosyltransferase from ***Streptococcus*** mutans by elution from water-insoluble polysaccharide with a dissociating solvent

AU ***Smith, Daniel J.*** ; Taubman, Martin A.; Ebersole, Jeffrey L.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, Mass., USA

SO Infect. Immun. (1979), 23(2), 446-52

CODEN: INFIBR; ISSN: 0019-9567

DT Journal

LA English

AB Glucosyltransferase (I) was obtained by dissocn. from water-insol. polysaccharide in the presence of 6M guanidine-HCl. Water-insol. polysaccharide was synthesized by cell-free culture supernatants from S. mutans strain 6715. Gel filtration of I on a column of 8% agarose in phosphate buffer, followed by filtration on a column of 4% crosslinked agarose in 6M guanidine-HCl, gave a 23-fold enrichment of the enzyme. The enriched I prepn. contained 22% carbohydrate and eluted at a position corresponding to a mol. wt. of 422,000. Polyacrylamide gel electrophoresis revealed 2 regions which stained for protein, formed water-insol. polysaccharide in the presence of sucrose, and pptd. with antisera directed to crude I preps. The guanidine-eluted enzyme could be primed by 5 .times. 10⁻⁵ M dextran T10. High-mol.-wt. glucan and a possible glucan-binding protein were also obtained after the final gel filtration step in addn. to I.

L2 ANSWER 37 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1980:4595 CAPLUS

DN 92:4595

TI Effect of oral administration of glucosyltransferase antigens on experimental dental caries

AU ***Smith, Daniel J.*** ; Taubman, Martin A.; Ebersole, Jeffrey L.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, MA, 02115, USA

SO Infect. Immun. (1979), 26(1), 82-9

CODEN: INFIBR; ISSN: 0019-9567

DT Journal

LA English

AB The effect of oral administration of sol. antigen preps. contg. glucosyltransferase on dental caries in hamsters was studied. Immunization was accomplished by feeding glucosyltransferase for 21 - 27 consecutive days. This immunization regimen resulted in the formation of salivary antibody, which was detected by functional inhibition of enzymic activity and by a modified enzyme-linked immunosorbent assay. A serum

response also occurred in 2 of the 3 expts. performed. After infection with cariogenic ***Streptococcus*** mutans strain 6715, glucosyltransferase-fed hamsters had significantly fewer S. mutans cells recoverable from molar surfaces on 6 of 9 occasions, compared with buffer-fed control groups. Hamsters orally immunized with glucosyltransferase also always had lower mean caries scores and mean nos. of lesions than comparably infected sham-immunized groups. Thus, significant protection from exptl. dental caries can be accomplished by oral administration of sol. antigen preps. contg. glucosyltransferase.

L2 ANSWER 38 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1980:162036 CAPLUS

DN 92:162036

TI The effects of local immunization with ***streptococcus*** mutans enzymic antigens on experimentally induced dental caries in rats

AU Taubman, Martin A.; ***Smith, Daniel J.*** ; Ebersole, Jeffrey L.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, MA, USA

SO Report (1978), NIDR/CR-79/05; Order No. PB-298912, 48 pp. Avail.: NTIS

From: Gov. Rep. Announce. Index (U. S.) 1979, 79(24), 78

DT Report

LA English

AB Immunization of rats with glucosyltransferase (GTF) from strain 6715 (PF6,7 and 9) or strain Ingbritt (PF10) or with whole cells from strains HS6, 6715 and Ingbritt (PF8) resulted in inhibition of GTF and radioactive GTF binding prior to infection and at the termination of these expts. Some redns. in S. mutans recovered were obsd. The homologous aspects of these observations were confirmed in germfree (G4) and hamster (H7) models. A degree of cross-protection was obsd. among serotypes of mutans when either whole cells (H8) or crude GFT antigens (PF9 and 10) were used for injection. GTF enzymes were prepd. from S. mutans strains E49 (serotype a), Ingbritt (serotype c) and 6715 (serotype g) by guanidine-HCl elution from water-insol. polysaccharide. GTF from S. mutans 6715 contained a single protein component and glucan. Immunization of hamsters with GTF from S. mutans E49 resulted in redns. in dental caries caused by homologous (E49) and heterologous (6715) serotypes and also redns. in S. mutans organisms recovered (H8). Tx rats immunized with whole cells had fewer caries and lesions than sham-immunized Tx rats but more disease than normal rats immunized in the same fashion. Thus, tx rats have a compensatory IgM response.

L2 ANSWER 39 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1979:101788 CAPLUS

DN 90:101788

TI Antibody binding of glucosyltransferase enzyme preparations from homologous and heterologous serotypes of S. mutans

AU Taubman, Martin A.; ***Smith, Daniel J.*** ; Ebersole, Jeffery L.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, Mass., USA

SO Adv. Exp. Med. Biol. (1978), 107(Secretory Immun. Infect.), 317-25

CODEN: AEMBAP; ISSN: 0065-2598

DT Journal

LA English

AB Rat salivary IgA and serum IgG antibodies to glucosyltransferase (GTF) from serotypes a, c, and g of ***Streptococcus*** mutans reacted with the serotypically unrelated (heterologous) GTF in enzyme- and radioimmunoassays. For example, the anti-serotype c GTF serum was

.apprx.66% cross-reactive with serotype g. However, salivary anti-serotype g had no effect on serotype c GTF enzyme activity. Immunization against dental caries is discussed.

L2 ANSWER 40 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1979:70442 CAPLUS

DN 90:70442

TI Cross-protective aspects of glucosyltransferase antigens in the hamster caries model

AU ***Smith, Daniel J.*** ; Taubman, Martin A.; Ebersole, Jeffrey L.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, Mass., USA

SO Adv. Exp. Med. Biol. (1978), 107(Secretory Immun. Infect.), 271-9

CODEN: AEMBAP; ISSN: 0065-2598

DT Journal

LA English

AB Glucosyltransferases (GTF) from ***Streptococcus*** mutans serotypes a and g were closely related antigenically but were more distantly related to GTF of serotype c. Local immunization with GTF from serotype c reduced the colonization, caries, and lesions caused by infection with the homologous strain compared with sham-injected controls. Local immunization with GTF of serotype c reduced the colonization, caries, and lesions caused by infection with S. mutans serotype g (strain 6715).

L2 ANSWER 41 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1977:119154 CAPLUS

DN 86:119154

TI Effects of local immunization with glucosyltransferase fractions from ***Streptococcus*** mutans on dental caries in rats and hamsters

AU Taubman, Martin A.; ***Smith, Daniel J.***

CS Dep. Immunol., Forsyth Dent. Cent., Boston, Mass., USA

SO J. Immunol. (1977), 118(2), 710-20

CODEN: JOIMA3

DT Journal

LA English

AB The effect of local immunization with glucosyltransferase enzymes of S. mutans on dental caries in conventional rats, hamsters, and gnotobiotic rats was studied. Injection of these animals with crude or defined glucosyltransferase enzyme preps. incorporated into complete Freund's adjuvant consistently produced antibody in saliva demonstrable by functional inhibition of enzymatic activity and binding of radioactive enzyme. Serum antibody was also present. The immunized group of animals always had lower mean caries scores than comparably sham-immunized or nonimmunized control groups. Hamsters immunized with a defined enzyme prep., contg. no more than 3 antigenic components (2 of which were enzyme), also demonstrated significant redns. in mean caries scores. The nos. of lesions were also always lower in immunized animals. In some cases there were redns. in the nos. of S. mutans that could be recovered from the teeth of immunized, infected animals. The redns. in dental caries and lesions were greater on smooth dental surfaces than on occlusal surfaces, which might be explained as interference with adherence phenomena demonstrated by S. mutans. It is proposed that antibody interference affects dental caries caused by this organism.

L2 ANSWER 42 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1977:87568 CAPLUS

DN 86:87568

TI Antigenic relatedness of glucosyltransferase enzymes from
Streptococcus mutans

AU ***Smith, Daniel J.*** ; Taubman, Martin A.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, Mass., USA

SO Infect. Immun. (1977), 15(1), 91-103

CODEN: INFIBR

DT Journal

LA English

AB The antigenic relation of glucosyltransferases (GTF) produced by different serotypes of *S. mutans* was studied by using a functional inhibition assay. Rat, rabbit, or hamster immune fluids, directed to cell-assocd. or supernatant-derived GTF, were tested against (NH₄)₂SO₄-pptd. culture supernatants contg. GTF from 7 strains of *S. mutans* representing 6 different serotypes. An antigenic relationship was shown to exist among GTF from serotypes a, d, and g, since both rat and rabbit antisera directed to serotype a or g GTF inhibited GTF of serotypes d and g similarly and both antisera also inhibited serotype a GTF. Furthermore, serum inhibition patterns indicated that GTF of serotypes c and e, and possibly b, are antigenically related to each other, but are antigenically distinct from GTF of serotype a, d, or g. Serum antibody directed to antigens other than enzyme (e.g., serotype-specific antigen or teichoic acid) had little effect on the inhibition assay. Salivas from rats immunized with cell-assocd. or supernatant-derived GTF exhibited low but consistent inhibition of GTF activity, which generally corresponded to the serum patterns. The sera of 2 groups of hamsters immunized with GTF (serotype g), enriched either in water-insol. or water-sol. glucan synthetic activity, gave patterns of inhibition quite similar to those seen with sera from more heterogeneous cell-assocd. or crude supernatant-derived GTF preps. Both groups of hamster sera also gave virtually identical patterns, suggesting that the 2 enzyme forms used as antigen share common antigenic determinants. The results from the 3 animal models suggest that among the cariogenic organisms tested, 2 (serotypes a, d, g and b, c, e), or perhaps 3 (serotypes a, d, g; b; and c, e), different subsets of GTF exist that have distinct antigenic determinants within a subset.

L2 ANSWER 43 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1976:403672 CAPLUS

DN 85:3672

TI A spectrophotometric procedure for quantitation of antibody directed to bacterial antigens

AU Iacono, Vincent J.; Taubman, Martin A.; ***Smith, Daniel J.*** ;
Moreno, Edgard C.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, Mass., USA

SO Immunochemistry (1976), 13(3), 235-43

CODEN: IMCHAZ

DT Journal

LA English

AB A spectrophotometric procedure was used to study the interaction of 108 formalin-killed whole bacterial cells (***Streptococcus*** mutans 6715) with antibody (IgG 7.6-380 .mu.g/100 .mu.l) and to rapidly quantitate serum antibody directed to bacteria. The procedure was at least as accurate as other procedures, but had the advantage of permitting detns. to be made after 1 min of reaction.

L2 ANSWER 44 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1978:473991 CAPLUS

DN 89:73991

TI Structure and function of the type-specific polysaccharide of
Streptococcus mutans 6715

AU Iacono, Vincent J.; Taubman, Martin A.; ***Smith, Daniel J.*** ;
Garant, Philias R.; Pollock, Jerry J.

CS Dep. Periodontics, State Univ. New York, Stony Brook, N. Y., USA

SO Immunol. Aspects Dent. Caries, Proc. Workshop Sel. Immunogens Caries
Vaccine Cross React. Antisera Oral Microorg. Mamm. Tissues (1976), 75-90.

Editor(s): Bowen, William H.; Genco, Robert J.; O'Brien, Thomas C.

Publisher: Inf. Retr. Inc., Arlington, Va.

CODEN: 38NFA9

DT Conference; General Review

LA English

AB A review with 44 refs., of the title antigens discussing in addn. their
importance in serol. classification and adherence phenomena of the
bacteria.

L2 ANSWER 45 OF 45 CAPLUS COPYRIGHT 2002 ACS

AN 1975:96372 CAPLUS

DN 82:96372

TI Isolation and immunochemical characterization of the group-specific
antigen of ***Streptococcus*** mutans 6715

AU Iacono, Vincent J.; Taubman, Martin A.; ***Smith, Daniel J.*** ;
Levine, Michael J.

CS Sch. Dent. Med., Harvard Univ., Boston, Mass., USA

SO Infect. Immun. (1975), 11(1), 117-28

CODEN: INFIBR

DT Journal

LA English

AB The group d antigen of S. mutans 6715 was isolated from a buffer (pH
7.3)-boiled ext. of whole cells and analyzed immunochem. This presumptive
major antigen was found in culture supernatant, sonically treated
supernatant, acid and buffer exts. of whole cells, and trichloroacetic
acid ext. of cell membranes. A crude prepn. of this antigen could
completely inhibit antibody-mediated cell (S. mutans 6715) agglutination.
The antigen was purified from buffer-boiled exts. by gel filtration on
columns of Sepharose 4B. The antigen did not migrate to the anode on
electrophoresis nor did it contain appreciable quantities of P, glycerol,
or ribitol. This suggested that the d antigenicity did not reside in a
teichoic acid. The d antigen contained galactose and glucose as the sole
saccharides, in a ratio of 5.9:1.0. Protein (9.5%) appeared to be a
portion of the antigen, although Pronase-digested antigen retained the
same electrophoretic mobility and could ppt. virtually all (98.6%)
purified antibody directed to the intact antigen. The immunodominant
region of the d antigen was primarily dependent upon galactose. The
.beta.-1-linkage of this galactose might also be involved. Glucose also
contributed to the immunodominant region.

=> e taubman martin a/au

E1 149 TAUBMAN MARK B/AU

E2 1 TAUBMAN MARTIN/AU

E3 77 --> TAUBMAN MARTIN A/AU
 E4 1 TAUBMAN MATTHEW/AU
 E5 8 TAUBMAN MATTHEW S/AU
 E6 3 TAUBMAN MICHELE/AU
 E7 1 TAUBMAN MITCHELL/AU
 E8 1 TAUBMAN N A/AU
 E9 1 TAUBMAN NORA E/AU
 E10 1 TAUBMAN O/AU
 E11 11 TAUBMAN P/AU
 E12 2 TAUBMAN R/AU

=> s e2-e3 and streptoc?

L3 53 ("TAUBMAN MARTIN"/AU OR "TAUBMAN MARTIN A"/AU) AND STREPTOC?

=> dup rem l3

PROCESSING COMPLETED FOR L3

L4 40 DUP REM L3 (13 DUPLICATES REMOVED)

=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 40 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 2001:886776 CAPLUS

DN 136:36332

TI Synthetic peptide vaccines for dental caries

IN Smith, Daniel J.; ***Taubman, Martin A.***

PA USA

SO U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. 5,686,075.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001048926	A1	20011206	US 1997-967573	19971110
US 5686075	A	19971111	US 1993-57162	19930430
PRAI US 1992-877295	B2	19920501		
US 1993-57162	A2	19930430		

PI US 2001048926 A1 20011206 US 1997-967573 19971110

US 5686075 A 19971111 US 1993-57162 19930430

PRAI US 1992-877295 B2 19920501

US 1993-57162 A2 19930430

AB Vaccine compns. and immunogenic compns. are described which are glucosyltransferase subunit vaccines for dental caries and which contain at least one peptide which corresponds to a sequence of glucosyltransferase contg. aspartate 413, aspartate 415 or both aspartate 413 and aspartate 415. These subunit vaccines elicit antibodies which protect an immunized mammal from dental caries. Methods of provoking an immune response to intact glucosyltransferase are also described.

L4 ANSWER 2 OF 40 USPATFULL

AN 2001:223710 USPATFULL

TI SYNTHETIC PEPTIDE VACCINES FOR DENTAL CARIES

IN SMITH, DANIEL J., NATICK, MA, United States

TAUBMAN, MARTIN A., NEWTONVILLE, MA, United States

PI US 2001048926 A1 20011206

AI US 1997-967573 A1 19971110 (8)

RLI Continuation-in-part of Ser. No. US 1993-57162, filed on 30 Apr 1993,

GRANTED, Pat. No. US 5686075 Continuation-in-part of Ser. No. US
1992-877295, filed on 1 May 1992, ABANDONED

DT Utility

FS APPLICATION

LREP PATRICIA GRANAHAH, HAMILTON BROOK SMITH AND REYNOLDS, TWO MILITIA DRIVE,
LEXINGTON, MA, 02173

CLMN Number of Claims: 19

ECL Exemplary Claim: 1

DRWN 8 Drawing Page(s)

LN.CNT 804

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Vaccine compositions and immunogenic compositions are described which
are glucosyltransferase subunit vaccines for dental caries and which
contain at least one peptide which corresponds to a sequence of
glucosyltransferase containing aspartate 413, aspartate 415 or both
aspartate 413 and aspartate 415. These subunit vaccines elicit
antibodies which protect an immunized mammal from dental caries. Methods
of provoking an immune response to intact glucosyltransferase are also
described.

L4 ANSWER 3 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

1

AN 2001:397601 BIOSIS

DN PREV200100397601

TI Facilitated intranasal induction of mucosal and systemic immunity to
mutans ***streptococcal*** glucosyltransferase peptide vaccines.

AU Smith, Daniel J. (1); King, William F.; Barnes, Leigh A.; Trantolo, Debra;
Wise, Donald L.; ***Taubman, Martin A.***

CS (1) Department of Immunology, The Forsyth Institute, 140 The Fenway,
Boston, MA, 02115: dsmith@forsyth.org USA

SO Infection and Immunity, (August, 2001) Vol. 69, No. 8, pp. 4767-4773.
print.

ISSN: 0019-9567.

DT Article

LA English

SL English

AB Synthetic peptide vaccines which are derived from functional domains of
Streptococcus mutans glucosyltransferases (GTF) have been shown to
induce protective immunity in Sprague-Dawley rats after subcutaneous
injection in the salivary gland region. Since mucosal induction of
salivary immunity would be preferable in humans, we explored methods to
induce mucosal antibody in the rat to the GTF peptide vaccines HDS and
HDS-GLU after intranasal administration. Several methods of facilitation
of the immune response were studied: the incorporation of peptides in
bioadhesive poly(D,L-lactide-coglycolide) (PLGA) microparticles, the use
of monoepitopic (HDS) or diepitopic (HDS-GLU) peptide constructs, or the
use of mucosal adjuvants. Salivary immunoglobulin A (IgA) responses were
not detected after intranasal administration of diepitopic HDS-GLU peptide
constructs in alum or after incorporation into PLGA microparticles.
However, significant primary and secondary salivary IgA and serum IgG
antibody responses to HDS were induced in all rats when cholera holotoxin
(CT) or a detoxified mutant Escherichia coli heat-labile enterotoxin
(R192G LT) were intranasally administered with HDS peptide constructs in
PLGA. Coadministration of LT with HDS resulted in predominantly IgG2a
responses in the serum, while coadministration with CT resulted in

significant IgG1 and IgG2a responses to HDS. Serum IgG antibody, which was induced to the HDS peptide construct by coadministration with these adjuvants, also bound intact mutans ***streptococcal*** GTF in an enzyme-linked immunosorbent assay and inhibited its enzymatic activity. Thus, immune responses which are potentially protective for dental caries can be induced to peptide-based GTF vaccines after mucosal administration if combined with the CT or LT R192G mucosal adjuvant.

L4 ANSWER 4 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

2

AN 2001:337080 BIOSIS

DN PREV200100337080

TI Diepitopic construct of functionally and epitopically complementary peptides enhances immunogenicity, reactivity with glucosyltransferase, and protection from dental caries.

AU ***Taubman, Martin A. (1)*** ; Holmberg, Cynthia J.; Smith, Daniel J.

CS (1) Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA, 02115: mtaubman@forsyth.org USA

SO Infection and Immunity, (July, 2001) Vol. 69, No. 7, pp. 4210-4216. print. ISSN: 0019-9567.

DT Article

LA English

SL English

AB Coimmunization with peptide constructs from catalytic (CAT) and glucan-binding (GLU) domains of glucosyltransferase (GTF) of mutans ***streptococci*** has resulted in enhanced levels of antibody to the CAT construct and to GTF. We designed and synthesized a diepitopic construct (CAT-GLU) containing two copies of both CAT (B epitope only) and GLU (B and T epitope) peptides. The immunogenicity of this diepitopic construct was compared with that of individual CAT and GLU constructs by immunizing groups of Sprague-Dawley rats subcutaneously in the salivary gland vicinity with the CAT-GLU, CAT, or GLU construct or by treating rats by sham immunization. Levels of serum immunoglobulin G (IgG) antibody to GTF or CAT in the CAT-GLU group were significantly greater than in GLU- or CAT-immunized groups. Immunization with CAT-GLU was compared to coimmunization with a mixture of CAT and GLU in a second rodent experiment under a similar protocol. CAT-GLU immunization resulted in serum IgG and salivary IgA responses to GTF and CAT which were greater than after coimmunization. Immunization with the diepitopic construct and coimmunization with CAT and GLU constructs showed proliferation of T lymphocytes to GTF. Immunization with either the CAT or GLU construct has been shown to elicit significant protection in a rodent dental caries model. Similarly in this study, the enhanced response to GTF after immunization with the CAT-GLU construct resulted in protective effects on dental caries. Therefore, the CAT-GLU diepitopic construct can be a potentially important antigen for a caries vaccine, giving rise to greater immune response than after immunization with CAT, GLU, or a mixture of the two.

L4 ANSWER 5 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

3

AN 2000:222888 BIOSIS

DN PREV200000222888

TI Coimmunization with complementary glucosyltransferase peptides results in enhanced immunogenicity and protection against dental caries.

AU ***Taubman, Martin A. (1)*** ; Smith, Daniel J.; Holmberg, Cynthia J.; Eastcott, Jean W.

CS (1) Department of Immunology, Forsyth Institute, 140 The Fenway, Boston, MA, 02115 USA

SO Infection and Immunity, (May, 2000) Vol. 68, No. 5, pp. 2698-2703.
ISSN: 0019-9567.

DT Article

LA English

SL English

AB Peptide constructs from the catalytic (CAT) and glucan-binding (GLU) regions of the mutans ***streptococcal*** glucosyltransferase enzymes (GTF) can provide immunity to dental caries infection. A strategy of coimmunization was tested to determine whether protection could be enhanced. Rats were immunized with one of the previously described peptide constructs from the CAT or GLU region of the GTF of mutans ***streptococci*** or coimmunized with a combination of these constructs (CAT-GLU). Coimmunized animals demonstrated significantly higher serum immunoglobulin G (IgG) and salivary IgA antibody levels to CAT or GTF than rats immunized with either construct alone. To assess the functional significance of coimmunization with these constructs, animals were immunized as above or with ***Streptococcus*** sobrinus GTF and then infected with *S. sobrinus* to explore the effects of immunization on immunological, microbiological, and disease (dental caries) parameters. Serum antibody from the communized group inhibited *S. sobrinus* GTF-mediated insoluble glucan synthesis in vitro above that of the individual-construct-immunized groups. Immunization with CAT or GLU constructs resulted in significantly reduced dental caries after infection with *S. sobrinus* compared with sham-immunized animals. Coimmunization produced greater reductions in caries than after immunization with either CAT or GLU. Also, significant elevations in lymphocyte proliferative responses to CAT, GLU, and GTF were observed after coimmunization with CAT-GLU compared with the responses after immunization with the individual constructs. The results suggested that increased numbers of memory T cells, which could proliferate to CAT, were generated by coimmunization. The experiments support the functional significance of these GTF domains in dental caries pathogenesis and present coimmunization as a simple alternative to intact GTF to enhance protective immunity against cariogenic microorganisms.

L4 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1999:672601 CAPLUS

DN 131:298658

TI Conjugate vaccines for the prevention of dental caries

IN Lees, Andrew; ***Taubman, Martin A.*** ; Smith, Daniel J.

PA USA

SO PCT Int. Appl., 54 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9952548	A2	19991021	WO 1999-US7828	19990409
	WO 9952548	A3	19991202		
	W: AU, CA, JP				

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE

CA 2325338 AA 19991021 CA 1999-2325338 19990409

AU 9934864 A1 19991101 AU 1999-34864 19990409

EP 1069909 A2 20010124 EP 1999-916570 19990409

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI

PRAI US 1998-81315P P 19980410

WO 1999-US7828 W 19990409

AB The present invention provides glucan-based compns. and methods for stimulating an immune response against mutans ***Streptococci*** components and vaccines and methods for the treatment and prevention of dental caries. In a preferred embodiment, a glucan polymer is covalently bound to one or more T cell-dependent antigens to form a conjugate vaccine. The T cell-dependent antigen preferably contains epitopes of one or more mutans ***streptococcal*** proteins, such as a glucosyltransferase. Moreover, one or more moieties, including haptens, may be conjugated to the glucan or to the glucan-T cell-dependent compn. In a preferred embodiment, these moieties are peptides which contain immunogenic epitopes corresponding to components of a mutants ***streptococcus***.

L4 ANSWER 7 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

4

AN 1999:262698 BIOSIS

DN PREV199900262698

TI Antibody to glucosyltransferase induced by synthetic peptides associated with catalytic regions of alpha-amylases.

AU Smith, Daniel J. (1); Heschel, Rhonda L.; King, William F.; ***Taubman,***
*** Martin A.***

CS (1) Department of Immunology, Forsyth Dental Center, 140 The Fenway,
Boston, MA, 02115 USA

SO Infection and Immunity, (May, 1999) Vol. 67, No. 5, pp. 2638-2642.
ISSN: 0019-9567.

DT Article

LA English

SL English

AB We examined the immunogenicity and induction of inhibitory activity of 19-mer synthetic peptides which contained putative catalytic regions that were associated with the beta5 (EAW) and beta7 (HDS) strand elements of the suggested (beta, alpha)8 catalytic barrel domain of ***Streptococcus*** mutans glucosyltransferase (GTF). Both peptides readily induced serum immunoglobulin G (IgG) and salivary IgA antipeptide activity which was reactive both with the inciting peptide and with intact S. mutans GTF. Antisera to each peptide construct also inhibited the ability of S. mutans GTF to synthesize glucan. These observations support the existence of catalytic subdomains containing glutamate and tryptophan (EAW) or aspartate and histidine (HDS) residues, each of which have been suggested to be involved with the catalytic activity of GTF. Furthermore, the epitopes defined in these sequences have significant immunogenicity and can induce immune responses which interfere with GTF-mediated glucan synthesis.

L4 ANSWER 8 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2000:193149 BIOSIS

DN PREV200000193149

TI Microbiota of initial periodontitis in adults.

AU Tanner, Anne C. R. (1); ***Taubman, Martin A.***

CS (1) Department of Bioadhesion, Forsyth Institute, 140 The Fenway, Boston, MA, 02115 USA

SO Anaerobe, (June Aug., 1999) Vol. 5, No. 3-4, pp. 229-235.

ISSN: 1075-9964.

DT Article

LA English

SL English

AB This paper reviews our recent studies of the microbiota and host response of initial periodontitis. Understanding the initial stages of periodontitis will allow appropriate early treatment and prevention strategies. Our studies aimed to determine the major bacterial species that differentiated initial periodontitis from health, and evaluate whether subjects with initial periodontitis differed in serum IgG reactivity to putative initial periodontitis pathogens compared with healthy subjects. Initial periodontitis was characterized clinically using longitudinal periodontal attachment level measurements. Progressing periodontal loss was detected at interproximal (initial periodontitis), and buccal (progressing recession) locations from the study population of minimally periodontally diseased subjects. Initial periodontitis was characterized microbiologically by elevated proportions of *Bacteroides forsythus*, *Selenomonas noxia* and *Campylobacter rectus* when compared with non-periodontitis sites. The immunological checkerboard assay did not detect differences in serum IgG reactivity among healthy, gingivitis or initial periodontitis subjects, or changes in reactivity coincident with detection of initial periodontitis. Clinical, microbiological and immunological characterization of initial periodontitis was consistent with infection-associated Gram-negative anaerobic periodontal species. Progressing recession sites were colonized by *Actinomyces* and ****Streptococcus**** species, as were healthy sites. Progressing recession sites demonstrated periodontal loss that appeared unrelated to infection and appeared to be consistent with a traumatic tooth brushing etiology. Different types of lesions will require different approaches to therapy and prevention.

L4 ANSWER 9 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
5

AN 1998:505575 BIOSIS

DN PREV199800505575

TI Structural and antigenic characteristics of ****Streptococcus****
sobrinus glucan binding proteins.

AU Smith, Daniel J. (1); King, William F.; Wu, Christine D.; Shen, Bella I.;
Taubman, Martin A.

CS (1) Dep. Immunol., Forsyth Dent. Cent., 140 The Fenway, Boston, MA 02115
USA

SO Infection and Immunity, (Nov., 1998) Vol. 66, No. 11, pp. 5565-5569.

ISSN: 0019-9567.

DT Article

LA English

AB Three purified glucan binding proteins (GBP-2, GBP-3, and GBP-5) from ****Streptococcus**** *sobrinus* 6715 were compared structurally by mass spectroscopy of tryptic fragments and antigenically by Western blot analysis with rat antisera to each GBP or to peptides containing putative

glucan binding epitopes of mutans ***streptococcal***
 glucosyltransferases. Structural and antigenic analyses indicated that
 GBP-3 and GBP-5 are very similar but that both are essentially unrelated
 to GBP-2. None of these *S. sobrinus* GBPs appeared to have a strong
 antigenic relationship with GBPs from ***Streptococcus*** mutans.
 Thus, *S. sobrinus* GBP-2 and GBP-3 appear to be distinct proteins with
 potentially different functions. *S. sobrinus* GBP-5 may be a proteolytic
 fragment of GBP3, or, alternatively, the genes coding for these proteins
 may be closely related.

L4 ANSWER 10 OF 40 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6

AN 1997:735840 CAPLUS

DN 128:21853

TI Synthetic peptide vaccines for dental caries

IN ***Taubman, Martin A.*** ; Smith, Daniel J.

PA Forsyth Dental Infirmary for Children, USA

SO U.S., 11 pp. Cont.-in-part of U.S. Ser. No. 877,295, abandoned.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5686075	A	19971111	US 1993-57162	19930430
US 2001048926	A1	20011206	US 1997-967573	19971110
PRAI US 1992-877295	B2	19920501		
US 1993-57162	A2	19930430		

AB Immunization of animals with a compn. contg. either an amino acid sequence
 from the catalytic domain of glucosyltransferase, an amino acid sequence
 from the glucan-binding region of glucosyltransferase or an amino acid
 sequence from the native surface domain of glucosyltransferase provoke
 antibody and T-cell immune responses to this enzyme. Since this enzyme
 has been implicated in the colonization of mutans ***streptococci***
 on tooth surfaces, such immune responses are important for the prevention
 of dental caries. Multicomponent and multivalent compns. which include
 these amino acid sequences provide effective vaccine capabilities.

L4 ANSWER 11 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

7

AN 1997:515418 BIOSIS

DN PREV199799814621

TI Immunogenicity and protective immunity induced by synthetic peptides
 associated with a catalytic subdomain of mutans group

streptococcal glucosyltransferase.

AU Smith, Daniel J. (1); Shoushtari, Babak; Heschel, Rhonda L.; King, William
 F.; ***Taubman, Martin A.***

CS (1) Dep. Immunol., Forsyth Dent. Cent., 140 Fenway, Boston, MA 02115 USA

SO Infection and Immunity, (1997) Vol. 65, No. 11, pp. 4424-4430.

ISSN: 0019-9567.

DT Article

LA English

AB We examined the immunogenicity and induction of protective immunity of two
 19-mer sequences (GGY and AND) which overlapped a highly conserved region
 which has recently been implicated in the enzymatic activity of
 glucosyltransferases (GTFs) of the mutans group ***streptococci*** .

These peptides were synthesized as eight-branched constructs on a lysine core. Serum immunoglobulin G (IgG) antibody, induced by subcutaneous (s.c. (salivary gland vicinity)) injection with these peptide constructs, reacted with the inciting antigen, with mutants ***streptococcal*** GTFs, and with a 21-mer peptide (CAT) containing an aspartate previously shown to covalently bind sucrose. Several of these antisera also inhibited the ability of ***Streptococcus*** sobrinus GTF to synthesize insoluble glucan. Significant levels of salivary IgA antibody were also induced by GGY and AND peptide constructs after s.c. injection. The effect of immunization with the GGY and AND peptide constructs on the cariogenicity of ***Streptococcus*** mutants was studied in three experiments by immunization of weanling Sprague-Dawley rats, twice at 7- to 14-day intervals with peptides, S. sobrinus GTF, or phosphate-buffered saline. All rats were then orally infected with S. mutans SJ. After 63-day infection periods, the GGY and AND-injected groups had significant dental caries reductions compared with sham-injected groups in most experiments. These studies support the existence of an additional catalytic subdomain within the sequence defined by the GGY and AND peptides. Furthermore, the epitopes defined in these sequences have significant immunogenicity, can induce immune responses which interfere with GTF-mediated glucan synthesis in vitro, and can protect rats from experimental dental caries.

L4 ANSWER 12 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

8

AN 1996:438622 BIOSIS

DN PREV199699152228

TI Experimental immunization of rats with a ***Streptococcus*** mutants 59-kilodalton glucan-binding protein protects against dental caries.

AU Smith, Daniel J. (1); ***Taubman, Martin A.***

CS (1) Dep. Immunol., Forsyth Dent. Cent., Boston, MA 02115 USA

SO Infection and Immunity, (1996) Vol. 64, No. 8, pp. 3069-3073.

ISSN: 0019-9567.

DT Article

LA English

AB Glucan-binding proteins (GBPs) are theoretically important in the molecular pathogenesis of dental caries caused by ***Streptococcus*** mutants. The present study evaluated the ability of antibody induced by the S. mutans 59-kDa GBP (GBP-59) to affect dental caries caused by experimental infection with S. mutans in a rodent model. Groups of 20-day-old rats were injected twice at 9-day intervals subcutaneously in the salivary gland vicinity with GBP-59, glucosyltransferase (GTF), or phosphate-buffered saline (sham injection), each incorporated in an adjuvant. Two weeks after the second injection, GBP-59- and GTF-injected rats contained significant levels of salivary immunoglobulin A and serum immunoglobulin G antibody to the respective injected antigens. However, cross-reacting antibody to S. mutans GTF or GBP-59 was not induced by the respective antigen. Rats were then orally infected with S. mutans. After 71 days of infection, GBP-59- and GTF-injected groups had smaller numbers of S. mutans on their molar surfaces, compared with the sham-injected infected group. Total, sulcal, and smooth-surface molar caries in the GBP-59- and GTF-immunized S. mutans-infected groups were each significantly lower (P ltoreq 0.003) than the respective measures of caries in the sham injected infected group. The results of this investigation demonstrate that immunization with S. mutans GBP-59 induces an immune response in rats that can interfere with the accumulation of S.

mutans and can reduce the level of dental caries caused by this cariogenic ***streptococcus***. Furthermore, the protective immunity induced by either GBP-59 or GTF appears to result from antibodies to independent epitopes since these two S. mutans components do not have a close antigenic relationship.

L4 ANSWER 13 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

9

AN 1995:409470 BIOSIS

DN PREV199598423770

TI Immunization of rats with synthetic peptide constructs from the glucan-binding or catalytic region of mutans ***streptococcal*** glucosyltransferase protects against dental caries.

AU ***Taubman, Martin A. (1)*** ; Holmberg, Cynthia J.; Smith, Daniel J.

CS (1) Dep. Immunol., Forsyth Dental Center, Boston, MA 02115 USA

SO Infection and Immunity, (1995) Vol. 63, No. 8, pp. 3088-3093.

ISSN: 0019-9567.

DT Article

LA English

AB Previously, we have described peptide constructs from two regions of glucosyltransferase (GTF) of mutans ***streptococci***. A putative catalytic site in the amino-terminal half of the molecule and a repeated glucan-binding site in the carboxyl-terminal half of GTF were the regions upon which sequences were based. The present study explored the effects of immunization with these peptide constructs (called CAT or GLU) and with ***streptococcal*** GTFs from ***Streptococcus*** sobrinus and S. mutans on immunological, microbiological, and disease parameters. Groups of immunized Sprague-Dawley rats were infected with either 10⁸ S. sobrinus 6715 or 10⁸ S. mutans SJ32 organisms. Serum immunoglobulin G antibody levels, determined by enzyme-linked immunosorbent assay, to the respective peptide constructs and to the appropriate ***streptococcal*** GTF were significantly increased (after immunization) prior to infection and at the end of the experiment. Also, serum antibody from CAT-, GLU-, and S. sobrinus GTF-immunized rats inhibited S. sobrinus GTF-mediated insoluble glucan synthesis (all) and S. mutans GTF-mediated soluble glucan synthesis (all except anti-GLU) from sucrose. Immunization with the CAT or GLU peptide construct resulted in significantly reduced smooth surface and sulcal caries after infection with S. sobrinus. Sulcal dental caries after infection with S. mutans SJ32 were also significantly reduced in CAT- and GLU-immunized rats. Thus, immunization with peptides whose sequences are based on putative functional domains of mutans ***streptococcal*** GTF are protective toward a cariogenic S. sobrinus or S. mutans infection.

L4 ANSWER 14 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1995:970032 CAPLUS

DN 124:84183

TI Potential for glucosyltransferase-based synthetic peptides in a dental caries vaccine

AU Smith, Daniel J.; ***Taubman, Martin A.***

CS Department of Immunology, Forsyth Dental Center, Boston, MA, 02115, USA

SO Adv. Exp. Med. Biol. (1995), Volume Date 1995, 371B, 1157-9

CODEN: AEMBAP; ISSN: 0065-2598

DT Journal

LA English

AB The antigenicity and immunogenicity of MAP constructs contg. 4 copies of

peptides derived from sequences assocd. with the glucan-binding or catalytic domains of glucosyltransferase were studied in humans and rats. Both constructs reacted with several human serum IgG and salivary IgA antibody samples, and were immunogenic in rats, giving rise to high levels of anti-peptide serum IgG. These results are discussed in the context of developing a vaccine for dental caries.

L4 ANSWER 15 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1995:970029 CAPLUS

DN 124:53208

TI Development of salivary IgA antibody to oral ***streptococcal*** antigens associated with virulence

AU Smith, Daniel J.; ***Taubman, Martin A.***

CS Department of Immunology, Forsyth Dental Center, Boston, MA, 02115, USA

SO Adv. Exp. Med. Biol. (1995), Volume Date 1995, 371B, 1141-3

CODEN: AEMBAP; ISSN: 0065-2598

DT Journal

LA English

AB The authors studied the relationship between the initial infection with ***Streptococcus*** mutans and the appearance of the salivary antibody to ***streptococcal*** antigens that may be involved in colonization (glucosyltransferase, glucan-binding protein, and antigen I/II).

L4 ANSWER 16 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
10

AN 1995:39909 BIOSIS

DN PREV199598054209

TI Immunological Characteristics of a Synthetic Peptide Associated with a Catalytic Domain of Mutans ***Streptococcal*** Glucosyltransferase.

AU Smith, Daniel J. (1); ***Taubman, Martin A.*** ; King, William F.; Eida, Stephen; Powell, Jonathan R.; Eastcott, Jean

CS (1) Dep. Immunol., Forsyth Dent. Cent., Boston, MA 02115 USA

SO Infection and Immunity, (1994) Vol. 62, No. 12, pp. 5470-5476.

ISSN: 0019-9567.

DT Article

LA English

AB The immunogenicity of a multiple antigenic peptide construct consisting of four copies of the synthetic 21-mer peptide DANFDSIRVDAVDNVDADLLQ was measured. The composition of this peptide was derived from a sequence in the N-terminal region of mutans ***streptococcal*** glucosyltransferases (GTFs) containing an aspartic acid implicated in catalysis. The peptide (CAT) construct was synthesized as a tetramer on a lysine backbone and subcutaneously injected into Sprague-Dawley rats for polyclonal antibody formation or intraperitoneally injected into BALB/c mice, and then spleen cell fused with Sp2/OAg14 murine myeloma cells for monoclonal antibody formation. The resulting rat antisera and mouse monoclonal antibodies reacted with CAT and with native GTF isozymes from ***Streptococcus*** sobrinus and ***Streptococcus*** mutans (in enzyme-linked immunosorbent assay and Western blot (immunoblot) analyses). Functional inhibition of the water-insoluble glucan synthetic activity of *S. sobrinus* GTF-I was demonstrated with an immunoglobulin M anti-CAT monoclonal antibody (gt 80% inhibited) and with rat sera (approximately 17% inhibited). The monoclonal antibody preparation also modestly inhibited the water-soluble glucan synthetic activity of an *S. mutans* GTF mixture. These results suggest that the CAT peptide contains B-cell

epitopes that are similar to those of intact mutans ***streptococcal***
GTFs and has the potential to elicit antibody that can inhibit GTF
function. Thus, sequences within this peptide construct may have value for
inclusion in a synthetic dental caries vaccine.

L4 ANSWER 17 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

11

AN 1994:301149 BIOSIS

DN PREV199497314149

TI Purification and antigenicity of a novel glucan-binding protein of
Streptococcus mutans.

AU Smith, Daniel J. (1); Akita, Hirotoshi; King, William F.; ***Taubman,***
*** Martin A.***

CS (1) Dep. Immunol., Forsyth Dental Cent., 140 The Fenway, Boston, MA 02115
USA

SO Infection and Immunity, (1994) Vol. 62, No. 6, pp. 2545-2552.
ISSN: 0019-9567.

DT Article

LA English

AB A novel glucan-binding protein (GBP) having an apparent molecular mass of
59 kDa (GBP-59) has been purified from ***Streptococcus*** mutans SJ
by a combination of affinity chromatography on alpha-1,6-linked glucan,
gel filtration chromatography, and ion-exchange chromatography. GBP-59 was
distinct from the quantitatively predominant S. mutans GBP (GBP-74) on the
basis of size, elution position in a salt gradient, and antigenicity. Rat
antisera to purified GBP-59 and GBP-74 did not cross-react. GBP-59 is
apparently immunogenic in humans, since immunoglobulin A (IgA) antibody in
20 of 24 adult parotid saliva samples was shown to react with GBP-59 in an
enzyme-linked immunosorbent assay. The glucan-binding activity of GBP-59
was confirmed by anti-GBP-59 immunogold labelling of Sephadex G-50 that
had been preincubated with S. mutans culture supernatant. GBP-59 could be
detected in culture supernatants of all laboratory strains of S. mutans
(e.g., Ingbritt), as well as all strains of S. mutans that had been
recently isolated from young children. GBP-59 was often the only component
in protease inhibitor-containing 4-h S. mutans culture supernatants that
reacted with human parotid salivary IgA antibody in Western blot
(immunoblot) analyses. These studies suggest that GBP-59 is a structurally
and antigenically distinct S. mutans GBP that can elicit significant
levels of salivary IgA antibody in humans.

L4 ANSWER 18 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1994:86402 CAPLUS

DN 120:86402

TI Synthetic peptide vaccines for dental caries

IN ***Taubman, Martin A.*** ; Smith, Daniel J.

PA Forsyth Dental Infirmary for Children, USA

SO PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 9322341	A1	19931111	WO 1993-US4094	19930430
W: CA, JP				

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
EP 638092 A1 19950215 EP 1993-910953 19930430
R: BE, CH, DE, DK, FR, GB, IE, IT, LI, NL, SE
JP 07506374 T2 19950713 JP 1993-519549 19930430
PRAI US 1992-877295 A 19920501
WO 1993-US4094 W 19930430

AB Immunization of animals with a compn. contg. either an amino acid sequence from the catalytic domain, glucan-binding region, and native surface domain of glucosyltransferase (I) provoke antibody and T-cell immune responses to this enzyme. Since this enzyme has been implicated in the colonization of mutans ***streptococci*** on tooth surfaces, such immune responses are important for the prevention of dental caries. Sequences of synthetic I-derived peptides are included. The immunogenicity of the synthetic peptides was detd. in rats, as was reactivity of T and B lymphocytes to I in human.

L4 ANSWER 19 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
12

AN 1993:410070 BIOSIS

DN PREV199396075795

TI Antigenicity and immunogenicity of a synthetic peptide derived from a glucan-binding domain of mutans ***streptococcal*** glucosyltransferase.

AU Smith, Daniel J. (1); ***Taubman, Martin A.*** ; Holmberg, Cynthia F.; Eastcott, Jean; King, William F.; Ali-Salaam, Pia

CS (1) Dep. Immunol., Forsyth Dent. Cent., Boston, MA 02115 USA

SO Infection and Immunity, (1993) Vol. 61, No. 7, pp. 2899-2905.

ISSN: 0019-9567.

DT Article

LA English

AB The immunogenicity and antigenicity of a multiply antigenic peptide construct containing four copies of the synthetic peptide TGAQTIKGQKLYFKANGQQVKG were measured in rodents and humans, respectively. The composition of this peptide construct (termed GLU) was derived from a major repeating sequence in the C-terminal region of mutans ***streptococcal*** glucosyltransferases that synthesize water-insoluble glucan (GTF-I). The GLU peptide elicited high levels of serum immunoglobulin G antibody to GLU after subcutaneous injection into Sprague-Dawley rats. These antisera also reacted with intact GTF isozymes from ***Streptococcus*** sobrinus and ***Streptococcus*** mutans (by enzyme-linked immunosorbent assay (ELISA) and Western blot (immunoblot) analyses) and with an 87-kDa glucan-binding protein from S. sobrinus (by Western blot). The synthesis of filter-retained glucan by GTF-Sd of S. sobrinus could be inhibited (30%) by preincubation with anti-GLU rat serum. Splenic and lymph node lymphocytes from rats injected once with S. sobrinus GTF isozymes demonstrated significant proliferation after 5 days of culture with GLU. The GLU peptide reacted with 4 of 29 human parotid saliva samples and 5 of 29 human serum samples (by ELISA). These results suggest that the GLU peptide contains B- and T-cell epitopes that are similar to those of intact mutans ***streptococcal*** GTFs and possibly certain other glucan-binding proteins as well. Furthermore, since antibody to this epitope(s) appears to inhibit GTF function, sequences within this peptide construct may have value for inclusion in a synthetic dental caries vaccine.

L4 ANSWER 20 OF 40 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1993:470749 BIOSIS

DN PREV199345093874

TI Emergence of immune competence in saliva.

AU Smith, Daniel J. (1); ***Taubman, Martin A.***

CS (1) Dep. Immunol., Forsyth Dental Cent., Boston, MA 02115 USA

SO Critical Reviews in Oral Biology & Medicine, (1993) Vol. 4, No. 3-4, pp. 335-341.

Meeting Info.: Symposium on Contemporary Developments in Salivary Research

Buffalo, New York, USA November 6-10, 1991

ISSN: 1045-4411.

DT Article

LA English

L4 ANSWER 21 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1986:495855 CAPLUS

DN 105:95855

TI Caries immunity and immune responses to ***Streptococcus*** mutans glucosyltransferase

AU ***Taubman, Martin A.*** ; Smith, Daniel J.; Ebersole, Jeffrey L.; Stack, Wendy E.; Tsukuda, Tomio; Trocme, Marie C.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, MA, 02115, USA

SO Mol. Microbiol. Immunobiol. Streptococcus Mutans, Proc. Int. Conf. "Cell., Mol. Clin. Aspects Streptococcus Mutans" (1986), Meeting Date 1985, 279-86. Editor(s): Hamada, Shigeyuki. Publisher: Elsevier, Amsterdam, Neth.

CODEN: 55CZAF

DT Conference

LA English

AB Extirpation of Peyer's patches and/or mesenteric lymph nodes dramatically decreased the serum IgA response to S. mutans glucosyltransferase (GTF) in rats. Also, neonatally thymectomized or congenitally athymic rats produced little or no salivary antibody response to GTF. Athymic animals were more susceptible to dental caries than normal controls; however, immunization with anti-GTF antibodies reduced susceptibility to caries in both groups.

L4 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1984:435199 CAPLUS

DN 101:35199

TI Glucosyltransferase

IN ***Taubman, Martin A.*** ; Smith, Daniel J.

PA Forsyth Dental Infirmary for Children, USA

SO PCT Int. Appl., 12 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 8401170	A1	19840329	WO 1983-US1359	19830909
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W: JP, US

RW: AT, BE, CH, DE, FR, GB, LU, NL, SE

US 4438200	A	19840320	US 1982-416869	19820913
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CA 1183477	A1	19850305	CA 1983-420426	19830128
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EP 118547 A1 19840919 EP 1983-903053 19830909
EP 118547 B1 19910116
R: AT, BE, CH, DE, FR, GB, LI, NL, SE
JP 59501696 T2 19841011 JP 1983-503130 19830909
JP 04040989 B4 19920706
AT 60086 E 19910215 AT 1983-903053 19830909
PRAI US 1982-416869 19820913
EP 1983-903053 19830909
WO 1983-US1359 19830909

AB Glucosyltransferase (I) useful for immunization against dental caries is prepd. by culturing ***Streptococcus*** mutans in a medium contg. glucose and dialyzable nutrients and recovering I from the supernatant of the cultured cells by using a H₂O-insol. polyglucan matrix. I is concd. and purified by Sepharose CL-4B gel filtration using 6M guanidine-HCl for elution. Thus, I is prepd. from the supernatant of S. mutans cultures by admixing the supernatant with H₂O-insol. Sephadex beads prepd. by crosslinking dextrans of Leuconostoc mesenteroides with epichlorohydrin. After recovery and washing, the I-Sephadex bead complex is treated with a denaturing solvent (6M guanidine-HCl for 2 h at 37.degree.) to disrupt the complex and provide a I-denaturing solvent mixt.

L4 ANSWER 23 OF 40 USPATFULL

AN 84:15901 USPATFULL

TI Method for the preparation of glucosyltransferase

IN ***Taubman, Martin A.***, Newton, MA, United States

Smith, Daniel J., Natick, MA, United States

PA Forsyth Dental Infirmary for Children, Boston, MA, United States (U.S. corporation)

PI US 4438200 19840320

AI US 1982-416869 19820913 (6)

DT Utility

FS Granted

EXNAM Primary Examiner: Shapiro, Lionel M.

LREP Crowley, Richard P.

CLMN Number of Claims: 14

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 284

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method of preparing a purified glucosyltransferase (GTF) for use in immunization against dental caries, which method comprises: culturing a ***Streptococcus*** mutans in a medium containing glucose and dialyzable nutrients to form a mixture of culture cells and supernatant; recovering the supernatant by the removal of the culture cells; admixing the recovered supernatant with a water-insoluble, polymerized polysaccharide as solid particulate material for a period of time, to provide a GTF, solid particulate complex; recovering the GTF complex in solid particulate form by filtration; washing the solid GTF complex to remove unbound GTF and medium components; removing GTF from the solid particulate material by a denaturing solvent; recovering the water-insoluble particulate material for reuse in the method; and recovering the GTF from the water-insoluble polysaccharide and purifying the recovered GTF.

L4 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1984:470647 CAPLUS

DN 101:70647

TI Protective aspects of immune response to glucosyltransferase in relation to dental caries

AU ***Taubman, Martin A.*** ; Smith, Daniel J.; Ebersole, Jeffrey L.; Hillman, Jeffrey D.

CS Dep. Immunol., Forsyth. Dent. Cent., Boston, MA, 02115, USA

SO Glucosyltransferases, Glucans, Sucrose Dent. Caries, [Workshop] (1983), Meeting Date 1982, 249-58. Editor(s): Doyle, R. J.; Ciardi, J. E.

Publisher: IRL, Washington, D. C.

CODEN: 51ZJAK

DT Conference

LA English

AB Antibody to glucosyltransferase (GTF) can interfere with ***Streptococcus*** mutans accumulation in dental plaques both in vitro and in vivo. The redns. in caries subsequent to the interference with accumulation can be correlated with salivary IgA antibody. The redns. in caries or lesions extend beyond serotype boundaries. Studies of antibody to GTF in vitro provided extensive evidence demonstrating the mode of this antibody function in vivo. Antibody to S. mutans enhanced the permeability of plaque such that either diffusion of acid away from the surface and/or diffusion of buffer ions toward the surface was facilitated. Further studies with antibody to GTF-I indicated the water-insol. polyglucans (WIP) synthesized by GTF were preferentially inhibited and that water-sol.-polyglucans were not inhibited. Thus, immunol. interference with dental caries caused by S. mutans can now be explained on the mol. level. Antibody to GTF interferes with bacterial accumulation, and preferentially inhibits WIP synthesis. This inhibition results in a more porous plaque. Thus, the reduced levels of caries seen in immunized rodents could be the result of fewer bacteria secreting acid in a more porous plaque.

L4 ANSWER 25 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1984:470646 CAPLUS

DN 101:70646

TI Adjuvants, glucosyltransferase and caries vaccine

AU Ebersole, Jeffrey L.; ***Taubman, Martin A.*** ; Smith, Daniel J.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, MA, 02115, USA

SO Glucosyltransferases, Glucans, Sucrose Dent. Caries, [Workshop] (1983), Meeting Date 1982, 241-8. Editor(s): Doyle, R. J.; Ciardi, J. E.

Publisher: IRL, Washington, D. C.

CODEN: 51ZJAK

DT Conference

LA English

AB Regulation of salivary IgA (SIgA) responses to glucosyltransferase (GTF) from ***Streptococcus*** mutans was examd. in the rat. T-cell depletion of rat via neonatal thymectomy (Tx) resulted in a lack of ability to respond to GTF in soln. with SIgA antibodies. Likewise, the Tx rats exhibited a significantly decreased response to GTF when presented on the surface of S. mutans. Further studies indicated that particulate GTF antigen bound to its product (water-insol. polysaccharide) was more efficient at eliciting SIgA antibodies than sol. antigen. Studies of the effect of adjuvants on the SIgA antibody response showed that Al(OH)₃, complete Freund's adjuvant, and muramyl dipeptide enhanced SIgA antibody prodn. when injected locally or administered intragastrically.

L4 ANSWER 26 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1984:470645 CAPLUS

DN 101:70645

TI Antigenic relatedness of glucosyltransferases from ***Streptococcus*** mutans and ***Streptococcus*** sanguis

AU Smith, Daniel J.; ***Taubman, Martin A.*** ; Ebersole, Jeffrey L.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, MA, 02115, USA

SO Glucosyltransferases, Glucans, Sucrose Dent. Caries, [Workshop] (1983), Meeting Date 1982, 223-30. Editor(s): Doyle, R. J.; Ciardi, J. E. Publisher: IRL, Washington, D. C.

CODEN: 51ZJAK

DT Conference

LA English

AB The antigenic relationships among glucosyltransferases (GTF) from *S. mutans* were investigated using techniques measuring the binding of antibody to radiolabeled GTF or to GTF attached to polystyrene, or measuring the ability of antibody to inhibit GTF activity. IgG antibody to GTF from serotype c or g strains of *S. mutans* could bind to or inhibit the activity of GTF from homologous serotypes. However, IgG antibody to GTF from the g serotype reacted more strongly with GTF from serotypes a, d, and g than from serotypes c and e. Conversely, IgG antibody to GTF from the c serotype reacted best with GTF from serotypes c and e. Measurement of antibody activity in saliva generally revealed the same relationships. However, broad cross-protection was observed when these relationships were explored in vivo. The in vitro binding of IgG antibody to *S. mutans* GTF was low but significant for GTF from *S. sanguis* strains 10558, H7PR3, and 34. In vivo, significantly fewer rodents immunized with *S. mutans* GTF and subsequently challenged with *S. sanguis* H7PR3 remained infected compared with sham-immunized and challenged control groups. However, immunization with GTF from *S. sanguis* 34 did not influence the course of infection or disease after infection with cariogenic *S. mutans*.

L4 ANSWER 27 OF 40 USPATFULL

AN 81:8080 USPATFULL

TI Method of preparing a purified glucosyltransferase

IN ***Taubman, Martin A.*** , Newton, MA, United States

Smith, Daniel J., Natick, MA, United States

PA Forsyth Dental Infirmary for Children, Boston, MA, United States (U.S. corporation)

PI US 4250262 19810210

AI US 1979-103590 19791214 (6)

RLI Continuation of Ser. No. US 1978-956847, filed on 2 Nov 1978, now abandoned which is a division of Ser. No. US 1978-879432, filed on 21 Feb 1978, now patented, Pat. No. US 4150116, issued on 17 Apr 1979

DT Utility

FS Granted

EXNAM Primary Examiner: Shapiro, Lionel M.

LREP Crowley, Richard P.

CLMN Number of Claims: 13

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1795

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Immunization of animals with preparations containing more purified forms

of glucosyltransferase (GTF) results in the presence of antibody in saliva demonstrable by functional inhibitions of enzyme activity and binding of radioactive enzyme. Serum antibody was also present. Immunized groups of animals had lower mean caries scores than comparably sham-immunized or nonimmunized control groups. Local immunization with GTF of serotype c or g of a ***Streptococcus*** mutans reduces the colonization, caries, and lesions caused by infection with S. mutans of serotype g (strain 6715) or c, or with serotype g or c, or with serotype a or g, respectively.

L4 ANSWER 28 OF 40 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 13

AN 1979:454528 CAPLUS

DN 91:54528

TI Immunization against dental caries with glucosyltransferase antigens

IN ***Taubman, Martin A.*** ; Smith, Daniel J.

PA Forsyth Dental Infirmary for Children, USA

SO U.S., 18 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4150116	A	19790417	US 1978-879432	19780221
	CA 1152000	A1	19830816	CA 1979-322048	19790221
	US 4250262	A	19810210	US 1979-103590	19791214
PRAI	US 1978-879432		19780221		
	US 1978-956847		19781102		

AB Immunization of animals with preps. contg. bacterial glucosyltransferase resulted in the presence of antibody in saliva demonstrable by functional inhibition of enzyme activity and binding of radioactive enzyme. Serum antibody was also present. Immunized groups of animals had lower mean caries scores than comparably sham-immunized or nonimmunized control groups. Local immunization with glucosyltransferase of serotype c or g of a ***Streptococcus*** mutans reduced the colonization, caries, and lesions caused by infection with S. mutans of serotype g (strain 6715) or c, or with serotype g or c, or with serotype a or g, resp.

L4 ANSWER 29 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1979:163806 CAPLUS

DN 90:163806

TI Preparation of glucosyltransferase from ***Streptococcus*** mutans by elution from water-insoluble polysaccharide with a dissociating solvent

AU Smith, Daniel J.; ***Taubman, Martin A.*** ; Ebersole, Jeffrey L.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, Mass., USA

SO Infect. Immun. (1979), 23(2), 446-52

CODEN: INFIBR; ISSN: 0019-9567

DT Journal

LA English

AB Glucosyltransferase (I) was obtained by disocn. from water-insol. polysaccharide in the presence of 6M guanidine-HCl. Water-insol. polysaccharide was synthesized by cell-free culture supernatants from S. mutans strain 6715. Gel filtration of I on a column of 8% agarose in phosphate buffer, followed by filtration on a column of 4% crosslinked agarose in 6M guanidine-HCl, gave a 23-fold enrichment of the enzyme. The

enriched I prepn. contained 22% carbohydrate and eluted at a position corresponding to a mol. wt. of 422,000. Polyacrylamide gel electrophoresis revealed 2 regions which stained for protein, formed water-insol. polysaccharide in the presence of sucrose, and pptd. with antisera directed to crude I preps. The guanidine-eluted enzyme could be primed by 5 times. 10-5 M dextran T10. High-mol.-wt. glucan and a possible glucan-binding protein were also obtained after the final gel filtration step in addn. to I.

L4 ANSWER 30 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1980:4595 CAPLUS

DN 92:4595

TI Effect of oral administration of glucosyltransferase antigens on experimental dental caries

AU Smith, Daniel J.; ***Taubman, Martin A.*** ; Ebersole, Jeffrey L.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, MA, 02115, USA

SO Infect. Immun. (1979), 26(1), 82-9

CODEN: INFIBR; ISSN: 0019-9567

DT Journal

LA English

AB The effect of oral administration of sol. antigen preps. contg. glucosyltransferase on dental caries in hamsters was studied. Immunization was accomplished by feeding glucosyltransferase for 21 - 27 consecutive days. This immunization regimen resulted in the formation of salivary antibody, which was detected by functional inhibition of enzymic activity and by a modified enzyme-linked immunosorbent assay. A serum response also occurred in 2 of the 3 expts. performed. After infection with cariogenic ***Streptococcus*** mutans strain 6715, glucosyltransferase-fed hamsters had significantly fewer S. mutans cells recoverable from molar surfaces on 6 of 9 occasions, compared with buffer-fed control groups. Hamsters orally immunized with glucosyltransferase also always had lower mean caries scores and mean nos. of lesions than comparably infected sham-immunized groups. Thus, significant protection from exptl. dental caries can be accomplished by oral administration of sol. antigen preps. contg. glucosyltransferase.

L4 ANSWER 31 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1980:162036 CAPLUS

DN 92:162036

TI The effects of local immunization with ***streptococcus*** mutans enzymic antigens on experimentally induced dental caries in rats

AU ***Taubman, Martin A.*** ; Smith, Daniel J.; Ebersole, Jeffrey L.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, MA, USA

SO Report (1978), NIDR/CR-79/05; Order No. PB-298912, 48 pp. Avail.: NTIS

From: Gov. Rep. Announce. Index (U. S.) 1979, 79(24), 78

DT Report

LA English

AB Immunization of rats with glucosyltransferase (GTF) from strain 6715 (PF6,7 and 9) or strain Ingbritt (PF10) or with whole cells from strains HS6, 6715 and Ingbritt (PF8) resulted in inhibition of GTF and radioactive GTF binding prior to infection and at the termination of these expts. Some redns. in S. mutans recovered were obsd. The homologous aspects of these observations were confirmed in germfree (G4) and hamster (H7) models. A degree of cross-protection was obsd. among serotypes of mutans when either whole cells (H8) or crude GFT antigens (PF9 and 10) were used

for injection. GTF enzymes were prepd. from *S. mutans* strains E49 (serotype a), Ingbritt (serotype c) and 6715 (serotype g) by guanidine-HCl elution from water-insol. polysaccharide. GTF from *S. mutans* 6715 contained a single protein component and glucan. Immunization of hamsters with GTF from *S. mutans* E49 resulted in redns. in dental caries caused by homologous (E49) and heterologous (6715) serotypes and also redns. in *S. mutans* organisms recovered (H8). Tx rats immunized with whole cells had fewer caries and lesions than sham-immunized Tx rats but more disease than normal rats immunized in the same fashion. Thus, tx rats have a compensatory IgM response.

L4 ANSWER 32 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1979:101788 CAPLUS

DN 90:101788

TI Antibody binding of glucosyltransferase enzyme preparations from homologous and heterologous serotypes of *S. mutans*

AU ***Taubman, Martin A.*** ; Smith, Daniel J.; Ebersole, Jeffery L.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, Mass., USA

SO Adv. Exp. Med. Biol. (1978), 107(Secretory Immun. Infect.), 317-25

CODEN: AEMBAP; ISSN: 0065-2598

DT Journal

LA English

AB Rat salivary IgA and serum IgG antibodies to glucosyltransferase (GTF) from serotypes a, c, and g of ****Streptococcus**** mutans reacted with the serotypically unrelated (heterologous) GTF in enzyme- and radioimmunoassays. For example, the anti-serotype c GTF serum was .apprx.66% cross-reactive with serotype g. However, salivary anti-serotype g had no effect on serotype c GTF enzyme activity. Immunization against dental caries is discussed.

L4 ANSWER 33 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1979:70442 CAPLUS

DN 90:70442

TI Cross-protective aspects of glucosyltransferase antigens in the hamster caries model

AU Smith, Daniel J.; ***Taubman, Martin A.*** ; Ebersole, Jeffrey L.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, Mass., USA

SO Adv. Exp. Med. Biol. (1978), 107(Secretory Immun. Infect.), 271-9

CODEN: AEMBAP; ISSN: 0065-2598

DT Journal

LA English

AB Glucosyltransferases (GTF) from ****Streptococcus**** mutans serotypes a and g were closely related antigenically but were more distantly related to GTF of serotype c. Local immunization with GTF from serotype c reduced the colonization, caries, and lesions caused by infection with the homologous strain compared with sham-injected controls. Local immunization with GTF of serotype c reduced the colonization, caries, and lesions caused by infection with *S. mutans* serotype g (strain 6715).

L4 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1977:119154 CAPLUS

DN 86:119154

TI Effects of local immunization with glucosyltransferase fractions from ****Streptococcus**** mutans on dental caries in rats and hamsters

AU ***Taubman, Martin A.*** ; Smith, Daniel J.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, Mass., USA

SO J. Immunol. (1977), 118(2), 710-20

CODEN: JOIMA3

DT Journal

LA English

AB The effect of local immunization with glucosyltransferase enzymes of *S. mutans* on dental caries in conventional rats, hamsters, and gnotobiotic rats was studied. Injection of these animals with crude or defined glucosyltransferase enzyme preps. incorporated into complete Freund's adjuvant consistently produced antibody in saliva demonstrable by functional inhibition of enzymatic activity and binding of radioactive enzyme. Serum antibody was also present. The immunized group of animals always had lower mean caries scores than comparably sham-immunized or nonimmunized control groups. Hamsters immunized with a defined enzyme prep., contg. no more than 3 antigenic components (2 of which were enzyme), also demonstrated significant redns. in mean caries scores. The nos. of lesions were also always lower in immunized animals. In some cases there were redns. in the nos. of *S. mutans* that could be recovered from the teeth of immunized, infected animals. The redns. in dental caries and lesions were greater on smooth dental surfaces than on occlusal surfaces, which might be explained as interference with adherence phenomena demonstrated by *S. mutans*. It is proposed that antibody interference affects dental caries caused by this organism.

L4 ANSWER 35 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1977:87568 CAPLUS

DN 86:87568

TI Antigenic relatedness of glucosyltransferase enzymes from
Streptococcus mutans

AU Smith, Daniel J.; ***Taubman, Martin A.***

CS Dep. Immunol., Forsyth Dent. Cent., Boston, Mass., USA

SO Infect. Immun. (1977), 15(1), 91-103

CODEN: INFIBR

DT Journal

LA English

AB The antigenic relation of glucosyltransferases (GTF) produced by different serotypes of *S. mutans* was studied by using a functional inhibition assay. Rat, rabbit, or hamster immune fluids, directed to cell-assocd. or supernatant-derived GTF, were tested against (NH₄)₂SO₄-pptd. culture supernatants contg. GTF from 7 strains of *S. mutans* representing 6 different serotypes. An antigenic relationship was shown to exist among GTF from serotypes a, d, and g, since both rat and rabbit antisera directed to serotype a or g GTF inhibited GTF of serotypes d and g similarly and both antisera also inhibited serotype a GTF. Furthermore, serum inhibition patterns indicated that GTF of serotypes c and e, and possibly b, are antigenically related to each other, but are antigenically distinct from GTF of serotype a, d, or g. Serum antibody directed to antigens other than enzyme (e.g., serotype-specific antigen or teichoic acid) had little effect on the inhibition assay. Salivas from rats immunized with cell-assocd. or supernatant-derived GTF exhibited low but consistent inhibition of GTF activity, which generally corresponded to the serum patterns. The sera of 2 groups of hamsters immunized with GTF (serotype g), enriched either in water-insol. or water-sol. glucan synthetic activity, gave patterns of inhibition quite similar to those seen with sera from more heterogeneous cell-assocd. or crude

supernatant-derived GTF prepns. Both groups of hamster serums also gave virtually identical patterns, suggesting that the 2 enzyme forms used as antigen share common antigenic determinants. The results from the 3 animal models suggest that among the cariogenic organisms tested, 2 (serotypes a, d, g and b, c, e), or perhaps 3 (serotypes a, d, g; b; and c, e), different subsets of GTF exist that have distinct antigenic determinants within a subset.

L4 ANSWER 36 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1976:403672 CAPLUS

DN 85:3672

TI A spectrophotometric procedure for quantitation of antibody directed to bacterial antigens

AU Iacono, Vincent J.; ***Taubman, Martin A.*** ; Smith, Daniel J.; Moreno, Edgard C.

CS Dep. Immunol., Forsyth Dent. Cent., Boston, Mass., USA

SO Immunochemistry (1976), 13(3), 235-43

CODEN: IMCHAZ

DT Journal

LA English

AB A spectrophotometric procedure was used to study the interaction of 108 formalin-killed whole bacterial cells (***Streptococcus*** mutans 6715) with antibody (IgG 7.6-380 .mu.g/100 .mu.l) and to rapidly quantitate serum antibody directed to bacteria. The procedure was at least as accurate as other procedures, but had the advantage of permitting detns. to be made after 1 min of reaction.

L4 ANSWER 37 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1978:473991 CAPLUS

DN 89:73991

TI Structure and function of the type-specific polysaccharide of ***Streptococcus*** mutans 6715

AU Iacono, Vincent J.; ***Taubman, Martin A.*** ; Smith, Daniel J.; Garant, Philias R.; Pollock, Jerry J.

CS Dep. Periodontics, State Univ. New York, Stony Brook, N. Y., USA

SO Immunol. Aspects Dent. Caries, Proc. Workshop Sel. Immunogens Caries Vaccine Cross React. Antisera Oral Microorg. Mamm. Tissues (1976), 75-90.

Editor(s): Bowen, William H.; Genco, Robert J.; O'Brien, Thomas C.

Publisher: Inf. Retr. Inc., Arlington, Va.

CODEN: 38NFA9

DT Conference; General Review

LA English

AB A review with 44 refs., of the title antigens discussing in addn. their importance in serol. classification and adherence phenomena of the bacteria.

L4 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1975:96372 CAPLUS

DN 82:96372

TI Isolation and immunochemical characterization of the group-specific antigen of ***Streptococcus*** mutans 6715

AU Iacono, Vincent J.; ***Taubman, Martin A.*** ; Smith, Daniel J.; Levine, Michael J.

CS Sch. Dent. Med., Harvard Univ., Boston, Mass., USA

SO Infect. Immun. (1975), 11(1), 117-28

CODEN: INFIBR

DT Journal

LA English

AB The group d antigen of *S. mutans* 6715 was isolated from a buffer (pH 7.3)-boiled ext. of whole cells and analyzed immunochem. This presumptive major antigen was found in culture supernatant, sonically treated supernatant, acid and buffer exts. of whole cells, and trichloroacetic acid ext. of cell membranes. A crude prepn. of this antigen could completely inhibit antibody-mediated cell (*S. mutans* 6715) agglutination. The antigen was purified from buffer-boiled exts. by gel filtration on columns of Sepharose 4B. The antigen did not migrate to the anode on electrophoresis nor did it contain appreciable quantities of P, glycerol, or ribitol. This suggested that the d antigenicity did not reside in a teichoic acid. The d antigen contained galactose and glucose as the sole saccharides, in a ratio of 5.9:1.0. Protein (9.5%) appeared to be a portion of the antigen, although Pronase-digested antigen retained the same electrophoretic mobility and could ppt. virtually all (98.6%) purified antibody directed to the intact antigen. The immunodominant region of the d antigen was primarily dependent upon galactose. The .beta.-1-linkage of this galactose might also be involved. Glucose also contributed to the immunodominant region.

L4 ANSWER 39 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1975:71491 CAPLUS

DN 82:71491

TI Specificity of antibodies to ****Streptococcus**** mutans. Significance in inhibition of adherence

AU Genco, Robert J.; Evans, Richard T.; ***Taubman, Martin A.***

CS Sch. Dent., State Univ. New York, Buffalo, N. Y., USA

SO Adv. Exp. Med. Biol. (1974), 45, 327-36

CODEN: AEMBAP

DT Journal

LA English

AB Antiserum to *S. mutans* may inhibit adherence of the cells to smooth surfaces. This did not depend on bacterial death. Inhibition of adherence correlated with inhibition of cell-assocd. polysaccharide synthesis and inhibition of glucosyltransferase (I) activity. There was extensive cross reactivity between *S. mutans* strains of the Bratthall groups a and d. These 2 strains share an antigen (the a-d antigenic determinant). The finding that adherence and I activity of strain SL 1, a group d organism, was not inhibited with antisera to group a or d organism is considered esp. important, since this strain did not have the a-d antigenic determinant. Thus the a-d antigenic determinant may be important to adherence of *S. mutans* strains of group a and d. The in vivo significance of antibodies to cell surface antigens of *S. mutans* was examd. in rat expts. Immunized rats had salivary antibodies of the IgA class which inhibited the activity of homologous I enzymes. Thus the salivary IgA antibodies may interfere with *S. mutans* colonization of rat teeth by interfering with the synthesis of adherent dextrans.

L4 ANSWER 40 OF 40 CAPLUS COPYRIGHT 2002 ACS

AN 1972:84324 CAPLUS

DN 76:84324

TI Induction and properties of rabbit secretory .gamma.A antibody directed to group A ****streptococcal**** carbohydrate

AU ***Taubman, Martin A.*** ; Genco, Robert J.
 CS Sch. Dent., State Univ. New York, Buffalo, N. Y., USA
 SO Immunochemistry (1971), 8(12), 1137-55
 CODEN: IMCHAZ
 DT Journal
 LA English
 AB Secretory .gamma.A antibodies were induced in the colostrum of New Zealand Red rabbits by injection of Group A ***streptococcal*** vaccine into the mammary glands. Colostral antibodies were purified by elution from Group A cells used as solid immunoadsorbent. Antibodies of both the secretory .gamma.A and .gamma.G class were obtained upon elution with 5% N-acetyl-glucosamine (NAG) on pH 2.5 buffer. The eluates were filtered through Sepharose 6B to sep. the 11 S .gamma.A from the 7 S .gamma.G antibodies. From 4.2 to 13.1 .mu.g of .gamma.A/ml of original colostrum was obtained by elution with 5% NAG and from 20.4 to 208.8 .mu.g of .gamma.A/ml with pH 2.5 buffer. The amt. of .gamma.G antibody obtained in these eluates varied greatly, ranging from 90 to 10% of the total antibody recovered. Purified .gamma.A anti-NAG antibodies isolated from a single rabbit exhibited the following properties: (1) they agglutinated Group A cell walls. (2) They bound to Group A cell walls as demonstrated by indirect fluorescent antibody staining using monospecific fluoresceinlabeled goat anti-rabbit .gamma.A. (3) They failed to ppt. with Group A carbohydrate under conditions in which the .gamma.G anti-NAG antibody was found to ppt. (4) Secretory .gamma.A antibodies, however, inhibited the pptn. of the .gamma.G antibodies with Group A carbohydrate. (5) They contained secretory component as detected by gel diffusion tests. (6) The secretory .gamma.A antibodies bound tritiated p-nitrophenyl-.beta.-N-acetylglucosaminide in equil. dialysis expts. A plot of r (moles hapten bound/mole antibody) vs. c (M free hapten) for the binding of the hapten by .gamma.A antibodies shows that r increased with increasing hapten concn. and that there was a plateau as r approached 4, indicating that secretory .gamma.A may have a valence of 4. An assocn. const. of 105 l./mole could be estd. from the data; however, because of the low assocn. const., there was considerable scatter of points. The assocn. const. for .gamma.G anti-NAG, isolated from the same colostrum was about 1 log lower when tested with the same hapten. Neither .gamma.A or .gamma.G antibodies bound detectable amts. of tritiated N-acetylglucosamine, suggesting that the .beta.-linkage makes an important contribution to binding. Many of the properties described for secretory .gamma.A antibody can be explained by a preference of this antibody to bind most of its combining sites to a single mol. possessing multiple identical antigenic determinants as opposed to cross-linking 2 or more such mols. This property, termed monogamous polyvalency, could significantly enhance certain biol. functions of secretory .gamma.A.

=> s streptoc? and glucosyltransferase?

L5 3603 STREPTOC? AND GLUCOSYLTRANSFERASE?

=> s l5 and mutans

L6 2718 L5 AND MUTANS

=> s l5 and (glucosyltransferase b)

L7 65 L5 AND (GLUCOSYLTRANSFERASE B)

=> dup rem l7

PROCESSING COMPLETED FOR L7

L8 31 DUP REM L7 (34 DUPLICATES REMOVED)

=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 31 ANSWERS - CONTINUE? Y/(N):y

L8 ANSWER 1 OF 31 USPATFULL

AN 2002:54665 USPATFULL

TI Glucan-containing compositions and paper

IN Nichols, Scott E., Johnston, IA, UNITED STATES

PI US 2002031826 A1 20020314

AI US 2000-740274 A1 20001219 (9)

RLI Division of Ser. No. US 1998-210361, filed on 11 Dec 1998, PENDING

Continuation-in-part of Ser. No. US 1998-9620, filed on 20 Jan 1998,

GRANTED, Pat. No. US 6127603 Continuation-in-part of Ser. No. US

1998-7999, filed on 16 Jan 1998, GRANTED, Pat. No. US 6087559

Continuation-in-part of Ser. No. US 1998-8172, filed on 16 Jan 1998,

GRANTED, Pat. No. US 6127602 Continuation of Ser. No. US 1995-485243,

filed on 7 Jun 1995, GRANTED, Pat. No. US 5712107 Continuation of Ser.

No. US 1995-478704, filed on 7 Jun 1995, ABANDONED Continuation of Ser.

No. US 1995-482711, filed on 7 Jun 1995, ABANDONED

DT Utility

FS APPLICATION

LREP Catherine D. Brooke, Patent Agent, 7100 N.W. 62nd Avenue, P.O. Box 1000,

Johnston, IA, 50131-1000

CLMN Number of Claims: 34

ECL Exemplary Claim: 15

DRWN No Drawings

LN.CNT 3136

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides methods of making paper, utilizing glucans, produced by the ***glucosyltransferase*** ***B***, C or D enzyme of the species ***Streptococcus*** mutans, instead of modified starches. The present glucans are functionally similar to currently utilized modified starches and are particularly useful in the coating step of paper manufacture. The present glucans also exhibit thermoplastic properties and impart gloss to the paper during the coating step.

L8 ANSWER 2 OF 31 USPATFULL

AN 2002:38557 USPATFULL

TI Forages

IN Loiselle, Francois J., Clive, IA, UNITED STATES

Nichols, Scott E., Johnston, IA, UNITED STATES

Jenkins, Colin Leslie Dow, Evatt, AUSTRALIA

Simpson, Richard J., Murrumbateman, AUSTRALIA

PI US 2002023279 A1 20020221

AI US 2001-844408 A1 20010427 (9)

RLI Continuation of Ser. No. US 2000-653884, filed on 1 Sep 2000, ABANDONED

Continuation of Ser. No. US 1999-350649, filed on 9 Jul 1999, ABANDONED

Continuation-in-part of Ser. No. US 1997-979514, filed on 26 Nov 1997,

GRANTED, Pat. No. US 5985666 Continuation-in-part of Ser. No. US

1995-478704, filed on 7 Jun 1995, ABANDONED Continuation-in-part of Ser.

No. US 1995-485243, filed on 7 Jun 1995, GRANTED, Pat. No. US 5712107

Continuation-in-part of Ser. No. US 1995-482711, filed on 7 Jun 1995,
ABANDONED

DT Utility

FS APPLICATION

LREP Pioneer Hi-Bred International, Inc., Corporate Intellectual Property,
7100 N.W. 62nd Avenue, P.O. Box 1000, Johnston, IA, 50131-1000

CLMN Number of Claims: 6

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 607

AB A transgenic plant cell is provided containing a DNA molecule encoding an enzyme selected from the group consisting of fructosyltransferase, ***glucosyltransferase*** ***B***, mutants of ***glucosyltransferase*** ***B***, ***glucosyltransferase*** C, ***glucosyltransferase*** D, mutants of ***glucosyltransferase*** D and functional fragments of each enzyme. A transgenic plant regenerated from the plant cell is also provided. A method of improving the ensilability and the nutritional value of plants is also provided comprising introducing into the cells of the plant an expression cassette comprising the above DNA molecule operably linked to a promoter functional in the cells of the plant to yield transformed plant cells, and regenerating a transformed plant from the transformed cells. The transformed plants also provide improved digestibility in ruminants.

L8 ANSWER 3 OF 31 USPATFULL

AN 2002:33171 USPATFULL

TI Forages

IN Loisel, Francois J., Clive, IA, UNITED STATES

Nichols, Scott E., Johnson, IA, UNITED STATES

Jenkins, Colin Leslie Dow, Evatt, AUSTRALIA

Simpson, Richard J., Murrumbateman, AUSTRALIA

PI US 2002019997 A1 20020214

AI US 2001-879486 A1 20010612 (9)

RLI Continuation of Ser. No. US 2000-653885, filed on 1 Sep 2000, ABANDONED
Continuation of Ser. No. US 1999-350649, filed on 9 Jul 1999, ABANDONED
Continuation of Ser. No. US 1997-979514, filed on 26 Nov 1997, GRANTED,
Pat. No. US 5985666 Continuation-in-part of Ser. No. US 1995-478704,
filed on 7 Jun 1995, ABANDONED Continuation-in-part of Ser. No. US
1995-485243, filed on 7 Jun 1995, GRANTED, Pat. No. US 5712107
Continuation-in-part of Ser. No. US 1995-482711, filed on 7 Jun 1995,
ABANDONED

DT Utility

FS APPLICATION

LREP PIONEER HI-BRED INTERNATIONAL INC., 7100 N.W. 62ND AVENUE, P.O. BOX
1000, JOHNSTON, IA, 50131

CLMN Number of Claims: 13

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 625

AB A transgenic plant cell is provided containing a DNA molecule encoding an enzyme selected from the group consisting of fructosyltransferase, ***glucosyltransferase*** ***B***, mutants of ***glucosyltransferase*** ***B***, ***glucosyltransferase*** C, ***glucosyltransferase*** D, mutants of

glucosyltransferase D and functional fragments of each enzyme. A transgenic plant regenerated from the plant cell is also provided. A method of improving the ensilability and the nutritional value of plants is also provided comprising introducing into the cells of the plant an expression cassette comprising the above DNA molecule operably linked to a promoter functional in the cells of the plant to yield transformed plant cells, and regenerating a transformed plant from the transformed cells. The transformed plants also provide improved digestibility in ruminants.

L8 ANSWER 4 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

1

AN 2001:519303 BIOSIS

DN PREV200100519303

TI Substitutes for modified starch and latexes in paper manufacture.

AU Nichols, Scott E.

ASSIGNEE: Pioneer Hi-Bred International, Inc.

PI US 6284479 September 04, 2001

SO Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 4, 2001) Vol. 1250, No. 1, pp. No Pagination. e-file.

ISSN: 0098-1133.

DT Patent

LA English

AB The present invention provides methods of making paper, utilizing glucans, produced by the ***glucosyltransferase*** ***B***, C or D enzyme of the species ***Streptococcus*** mutans, instead of modified starches. The present glucans are functionally similar to currently utilized modified starches and are particularly useful in the coating step of paper manufacture. The present glucans also exhibit thermoplastic properties and impart gloss to the paper during the coating step.

L8 ANSWER 5 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

2

AN 2001:163077 BIOSIS

DN PREV200100163077

TI Plant cells and plants transformed with ***Streptococcus*** mutans genes encoding wild-type or mutant ***glucosyltransferase*** ***B*** enzymes.

AU Nichols, Scott E. (1)

CS (1) Johnston, IA USA

ASSIGNEE: Pioneer Hi-Bred International, Inc.

PI US 6087559 July 11, 2000

SO Official Gazette of the United States Patent and Trademark Office Patents, (July 11, 2000) Vol. 1236, No. 2, pp. No Pagination. e-file.

ISSN: 0098-1133.

DT Patent

LA English

AB The present invention provides methods of making paper utilizing glucans, produced by ***glucosyltransferase*** ***B*** enzymes of the species ***Streptococcus*** mutans, instead of modified starches. The present glucans are functionally similar to the hydroxethyl modified starch and are particularly useful in the sizing and coating steps of paper manufacture. The present glucans also exhibit thermoplastic properties and impart gloss to the paper during the coating step. In particular, the present invention provides plant cells and plants

transformed with ***Streptococcus*** mutans genes encoding wild-type or mutant ***glucosyltransferase*** ***B*** enzymes.

L8 ANSWER 6 OF 31 LIFESCI COPYRIGHT 2002 CSA

AN 2001:33393 LIFESCI

TI Plant cells and plants transformed with ***Streptococcus*** mutans genes encoding wild-type or mutant ***glucosyltransferase*** ***B*** enzymes

AU Nichols, S.E.

CS Pioneer Hi-Bred International, Inc.

SO (20000711) . US Patent: 6087559; US CLASS: 800/284; 435/69.7; 435/69.8; 435/100; 435/101; 435/193; 435/412; 435/417; 435/419; 435/468; 435/469; 435/470; 800/278; 800/287; 800/288; 800/292; 800/293; 800/294; 800/298; 800/317.2; 800/320; 800/320.1; 800/320.2; 800/320.3.

DT Patent

FS W2

LA English

SL English

AB The present invention provides methods of making paper utilizing glucans, produced by ***glucosyltransferase*** ***B*** enzymes of the species ***Streptococcus*** mutans, instead of modified starches. The present glucans are functionally similar to the hydroxethyl modified starch and are particularly useful in the sizing and coating steps of paper manufacture. The present glucans also exhibit thermoplastic properties and impart gloss to the paper during the coating step. In particular, the present invention provides plant cells and plants transformed with ***Streptococcus*** mutans genes encoding wild-type or mutant ***glucosyltransferase*** ***B*** enzymes.

L8 ANSWER 7 OF 31 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3

AN 1999:733006 CAPLUS

DN 131:333008

TI Transgenic plants contg. glycosyltransferase genes from ***Streptococcus*** mutans for improved forages

IN Loiselle, Francois J.; Nichols, Scott E.

PA Pioneer Hi-Bred International, Inc., USA

SO U.S., 6 pp., Cont.-in-part of U.S. Ser. No. 478,704, abandoned.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT.3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI US 5985666	A	19991116	US 1997-979514	19971126
US 5712107	A	19980127	US 1995-485243	19950607
AU 709402	B2	19990826	AU 1997-48460	19971218
AU 9748460	A1	19990617		

PRAI US 1995-478704 B2 19950607

US 1995-482711 B2 19950607

US 1995-485243 A2 19950607

AB A transgenic plant cell is provided contg. a DNA mol. encoding an enzyme selected from the group consisting of fructosyltransferase,

glucosyltransferase ***B***, mutants of

glucosyltransferase ***B***, ***glucosyltransferase*** C,

glucosyltransferase D, mutants of ***glucosyltransferase*** D

and functional fragments of each enzyme. A transgenic plant regenerated from the plant cell is also provided. A method of improving the ensilability and the nutritional value of plants is also provided comprising introducing into the cells of the plant an expression cassette comprising the above DNA mol. operably linked to a promoter functional in the cells of the plant to yield transformed plant cells, and regenerating a transformed plant from the transformed cells. The transformed plants also provide improved digestibility in ruminants.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 31 CAPLUS COPYRIGHT 2002 ACS

AN 1999:349364 CAPLUS

DN 131:124939

TI Inhibitory effect of a self-derived peptide on ***glucosyltransferase***
of ***Streptococcus*** mutans, Possible novel anticaries measures

AU Eto, Akiko; Saido, Takaomi C.; Fukushima, Kazuo; Tomioka, Shigeo; Imai, Susumu; Nisizawa, Tosiki; Hanada, Nobuhiro

CS Department of Oral Science, National Institute of Infectious Diseases,
Tokyo, 162-8640, Japan

SO J. Biol. Chem. (1999), 274(22), 15797-15802

CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

AB ***Glucosyltransferase*** (GTF) plays an important role in the development of dental caries. We examd. the possible presence of self-inhibitory segments within the enzyme mol. for the purpose of developing anticaries measures through GTF inhibition. Twenty-two synthetic peptides derived from various regions presumably responsible for insol.-glucan synthesis were studied with respect to their effects on catalytic activity. One of them, which is identical in amino acid sequence to residues 1176-1194, significantly and specifically inhibited both sucrose hydrolysis and glucosyl transfer to glucan by GTF-I. Double-reciprocal anal. revealed that the inhibition is noncompetitive. Scramble peptides, composed of the identical amino acids in randomized sequence, had no effect on GTF-I activity. Furthermore, the peptide is tightly bound to the enzyme once complexed, even in the presence of sodium dodecyl sulfate (SDS). Kinetic anal. using an optical evanescent resonant mirror cuvette system demonstrated that the enzyme-peptide interaction was biphasic. These results indicate that the peptide directly interacts with the enzyme with high affinity and inhibits its activity in a sequence-specific manner. This peptide itself could possibly be an effective agent for prevention of dental caries, although its effectiveness may be improved by further modification.

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

4

AN 1998:258263 BIOSIS

DN PREV199800258263

TI Inactivation of the gbpA gene of ***Streptococcus*** mutans increases virulence and promotes in vivo accumulation of recombinations between the ***glucosyltransferase*** ***B*** and C genes.

AU Hazlett, Karsten R. O. (1); Michalek, Suzanne M.; Banas, Jeffrey A.
CS (1) Dep. Microbiol., Immunol., Molecular Genetics, Albany Med. Coll.,
Albany, NY 12208 USA
SO Infection and Immunity, (May, 1998) Vol. 66, No. 5, pp. 2180-2185.
ISSN: 0019-9567.

DT Article

LA English

AB Glucan-binding protein A (GbpA) of ***Streptococcus*** mutans has been hypothesized to promote sucrose. dependent adherence and the cohesiveness of plaque and therefore to contribute to caries formation. We have analyzed the adherence properties and virulence of isogenic gbpA mutants relative to those of wild-type S. mutans. Contrary to expectations, the gbpA mutant strains displayed enhanced sucrose-dependent adherence in vitro and enhanced cariogenicity in vivo. In vitro, S. mutans was grown in the presence of (3H)thymidine and sucrose within glass vials. When grown with constant rotation, significantly higher levels of gbpA mutant organisms than of wild type remained adherent to the vial walls. Postgrowth vortexing of rotated cultures significantly decreased adherence of wild-type organisms, whereas the adherence of gbpA mutant organisms was unaffected. In the gnotobiotic rat model, the gbpA mutant strain was hypercariogenic though the colonization levels were not significantly different from those of the wild type. The gbpA mutant strain became enriched in vivo with organisms that had undergone a recombination involving the gtfB and gtfC genes. The incidence of gtfBC recombinant organisms increased as a function of dietary sucrose availability and was inversely correlated with caries development. We propose that the absence of GbpA elevates the cariogenic potential of S. mutans by altering the structure of plaque. However, the hypercariogenic plaque generated by gbpA mutant organisms may be suboptimal for S. mutans, leading to the accumulation of gtfBC recombinants whose reduced ***glucosyltransferase*** activity restores a less cariogenic plaque structure.

L8 ANSWER 10 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
5

AN 1998:268616 BIOSIS

DN PREV199800268616

TI Binding properties of ***streptococcal*** ***glucosyltransferases***
for hydroxyapatite, saliva-coated hydroxyapatite, and bacterial surfaces.

AU Vacca-Smith, A. M. (1); Bowen, W. H.

CS (1) Dep. Dent. Res., Rochester Caries Res. Cent., Univ. Rochester, 601
Elmwood Ave., Box 611, Rochester, NY 14642 USA

SO Archives of Oral Biology, (Feb., 1998) Vol. 43, No. 2, pp. 103-110.
ISSN: 0003-9969.

DT Article

LA English

AB The binding specificities of ***Streptococcus***
glucosyltransferase (Gtf) B, C and D for hydroxyapatite (HA),
saliva-coated hydroxyapatite (SHA), and bacterial surfaces were examined.
For HA beads the following values were obtained: (K = affinity; N = number
of binding sites) GtfB, K = 46×10^5 ml/mumol, N = 0.65×10^{-6} mumol/m²;
GtfC, K = 86×10^5 ml/mumol, N = 4.42×10^{-6} mumol/m²; GtfD, K = 100×10^5
ml/mumol, N = 0.83×10^{-6} mumol/m². For SHA beads, the following values
were obtained: GtfB, K = 14.7×10^5 ml/mumol, N = 1.03×10^{-6} mumol/m²;
GtfC, K = 21.3×10^5 ml/mumol, N = 3.66×10^{-6} mumol/m²; GtfD, K = $1.73 \times$

105 ml/mumol, $N = 8.88 \times 10^{-6}$ mumol/m². The binding of GtfB to SHA beads was reduced in the presence of parotid saliva, but the binding of GtfC and D was unaffected. The binding of GtfB to SHA in the presence of parotid saliva supplemented with GtfC and D was reduced when compared with its binding to SHA in the presence of parotid saliva alone. In contrast, the binding of GtfC and D to SHA was unaffected when parotid saliva was supplemented with the other Gtf enzymes. GtfB bound to several bacterial strains (*Strep. mutans* GS-5, *Actinomyces viscosus* OMZ105E and *Lactobacillus casei* 4646) in an active form, while GtfC and D did not bind to bacterial surfaces. It is concluded that of the three Gtf enzymes, GtfC has the highest affinity for HA and SHA surfaces and can adsorb on to the SHA surface in the presence of the other two enzymes. GtfD also binds to SHA in the presence of the other enzymes but has a very low affinity for the surface. GtfB does not bind to SHA in the presence of the other Gtf enzymes but binds avidly to bacterial surfaces in an active form. Therefore, GtfC most probably binds to apatitic surfaces, while GtfB binds to bacterial surfaces.

L8 ANSWER 11 OF 31 CAPLUS COPYRIGHT 2002 ACS

AN 1998:15893 CAPLUS

DN 128:76772

TI Substitutes for modified starch in paper manufacture

IN Nichols, Scott E.

PA Pioneer Hi-Bred International, Inc., USA

SO PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9747806	A1	19971218	WO 1996-US10190	19960612
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9662767	A1	19980107	AU 1996-62767	19960612
AU 731229	B2	20010329		
EP 904452	A1	19990331	EP 1996-921569	19960612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1048730	A2	20001102	EP 2000-110805	19960612
EP 1048730	A3	20001129		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001503607	T2	20010321	JP 1998-501538	19960612
PRAI EP 1996-921569	A3	19960612		
WO 1996-US10190	W	19960612		
AB A method of making paper utilizing glucans, produced by the ***glucosyltransferase*** ***B*** enzyme of the species ***Streptococcus*** mutans, instead of modified starches, is disclosed.				

The glucans are functionally similar to the hydroxethyl modified starch and are particularly useful in the coating and sizing step of paper manuf. The present glucans also exhibit thermoplastic properties and impart gloss to the paper during the coating step.

L8 ANSWER 12 OF 31 USPATFULL
AN 97:104112 USPATFULL
TI Oral immunization by transgenic plants
IN Curtiss, III, Roy, St. Louis, MO, United States
Cardineau, Guy A., Madison, WI, United States
PA Washington University, St. Louis, MO, United States (U.S. corporation)
PI US 5686079 19971111
AI US 1995-457563 19950601 (8)
RLI Division of Ser. No. US 1989-398520, filed on 29 Aug 1989 which is a continuation-in-part of Ser. No. US 1988-240728, filed on 6 Sep 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Housel, James C.; Assistant Examiner: Ryan, Verlene
LREP Saliwanchik, Lloyd & Saliwanchik
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 15 Drawing Page(s)
LN.CNT 1916
AB The invention is directed to transgenic plants expressing colonization and/or virulence antigens specified by genes from pathogenic microorganisms. It is also directed to the use of such transgenic plants for oral immunization of humans and other animals to elicit a secretory immune response which inhibits colonization of or invasion by such pathogenic microorganisms through a mucosal surface of humans or other animals.

L8 ANSWER 13 OF 31 USPATFULL
AN 97:97065 USPATFULL
TI Oral immunization by transgenic plants
IN Curtiss, III, Roy, St. Louis, MO, United States
Cardineau, Guy A., Madison, WI, United States
PA Washington University, St. Louis, MO, United States (U.S. corporation)
PI US 5679880 19971021
AI US 1995-457928 19950601 (8)
RLI Continuation of Ser. No. US 1989-398520, filed on 29 Aug 1989 which is a continuation-in-part of Ser. No. US 1988-240728, filed on 6 Sep 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Moody, Patricia R.
LREP Saliwanchik, Lloyd & Saliwanchik
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 15 Drawing Page(s)
LN.CNT 1933
AB The invention is directed to transgenic plants expressing colonization and/or virulence antigens specified by genes from pathogenic microorganisms. It is also directed to the use of such transgenic plants for oral immunization of humans and other animals to elicit a secretory

immune response which inhibits colonization of or invasion by such pathogenic microorganisms through a mucosal surface of humans or other animals.

L8 ANSWER 14 OF 31 USPATFULL
AN 97:68356 USPATFULL
TI Oral immunization by transgenic plants
IN Curtiss, III, Roy, St. Louis, MO, United States
Cardineau, Guy A., Madison, WI, United States
PA Washington University, St. Louis, MO, United States (U.S. corporation)
PI US 5654184 19970805
AI US 1995-458097 19950601 (8)
RLI Division of Ser. No. US 1989-398520, filed on 29 Aug 1989 which is a continuation-in-part of Ser. No. US 1988-240728, filed on 6 Sep 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Moody, Patricia R.
LREP Saliwanchik, Lloyd & Saliwanchik
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 15 Drawing Page(s)
LN.CNT 1883

AB The invention is directed to transgenic plants expressing colonization and/or virulence antigens specified by genes from pathogenic microorganisms. It is also directed to the use of such transgenic plants for oral immunization of humans and other animals to elicit a secretory immune response which inhibits colonization of or invasion by such pathogenic microorganisms through a mucosal surface of humans or other animals.

L8 ANSWER 15 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1997:157351 BIOSIS
DN PREV199799456554
TI Antigenicity of a synthetic peptide from ***glucosyltransferases*** of ***Streptococcus*** mutans in humans.
AU Chia, Jean-San (1); Lin, Shu-Wha; Yang, Czau-Siung; Chen, Jen-Yang
CS (1) Graduate Inst. Microbiol., Coll. Med., Natl. Taiwan Univ., No. 1, Jen Ai Road 1st Section, Taipei Taiwan
SO Infection and Immunity, (1997) Vol. 65, No. 3, pp. 1126-1130.
ISSN: 0019-9567.

DT Article
LA English
AB Human salivary immunoglobulin A (IgA) and serum IgG antibodies to the ***Streptococcus*** mutans ***glucosyltransferases*** (Gtfs) and to a synthetic peptide of 19 amino acids from a conserved region in the Gtfs (residues 435 to 453) were determined in young adults by enzyme-linked immunosorbent assay. Varying levels of antibody to Gtfs were detected in saliva or serum, with significantly higher levels of antibody to Gtfd than to Gtfb/C or Gtfc. Anti-Gtf IgA levels in saliva did not correlate with those of IgG in serum. Caries-free (CF) volunteers exhibited significantly higher salivary IgA antibody levels to the peptide and to Gtfb/C or Gtfc than did the caries-active (CA) subjects. Preincubation of CF saliva and serum with the peptide inhibited the antibodies to the Gtfs in a dose-dependent manner, whereas preincubation of the samples from the CA

group resulted in only partial inhibition. Our results indicated that this 19-amino-acid peptide includes one of the major B-cell epitopes of Gtfs and that CF individuals have higher titers of antibodies than CA subjects.

L8 ANSWER 16 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1997:283027 BIOSIS

DN PREV199799582230

TI Construction of ***glucosyltransferase*** ***B*** -cholera toxin A2/B chimeric proteins.

AU Jespersgaard, C.; Hajishengallis, G.; Smith, D. J.; Russell, M. W.; Michalek, S. M.

CS Dep. Microbiol., Univ. Alabama at Birmingham, Birmingham, AL USA

SO Abstracts of the General Meeting of the American Society for Microbiology, (1997) Vol. 97, No. 0, pp. 256.

Meeting Info.: 97th General Meeting of the American Society for

Microbiology Miami Beach, Florida, USA May 4-8, 1997

ISSN: 1060-2011.

DT Conference; Abstract; Conference

LA English

L8 ANSWER 17 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1997:282926 BIOSIS

DN PREV199799582129

TI Analysis of the S. mutans gtf B and C genes recombination product GTF BC.

AU Hazlett, Karsten (1); Michalek, Suzanne; Banas, Jeff (1)

CS (1) Dep. Microbiol., Albany Med. College, Albany, NY USA

SO Abstracts of the General Meeting of the American Society for Microbiology, (1997) Vol. 97, No. 0, pp. 238.

Meeting Info.: 97th General Meeting of the American Society for

Microbiology Miami Beach, Florida, USA May 4-8, 1997

ISSN: 1060-2011.

DT Conference; Abstract; Conference

LA English

L8 ANSWER 18 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1996:280414 BIOSIS

DN PREV199699002770

TI Interactions of ***streptococcal*** ***glucosyltransferases*** with alpha-amylase and starch on the surface of saliva-coated hydroxyapatite.

AU Vacca-Smith, A. M.; Venkitaraman, A. R.; Quivey., R. G., Jr.; Bowen, W. H. (1)

CS (1) Dep. Dental Res., Rochester Caries Res. Cent., Univ. Rochester, 601 Elmwood Aveune, Box 611, Rochester, NY 14642 USA

SO Archives of Oral Biology, (1996) Vol. 41, No. 3, pp. 291-298.

ISSN: 0003-9969.

DT Article

LA English

AB The salivary pellicle consists of various proteins and glycoproteins which may interact with one another. Experiments were performed to elucidate the interactions of ***streptococcal*** ***glucosyltransferase*** (Gtf) enzymes with human salivary alpha-amylase in solution and on the surface of saliva-coated hydroxyapatite (SHA) beads. The Gtf enzymes -B, -C and -D, when immobilized on to SHA beads, reduced the activity of adsorbed amylase; GtfD showed the highest inhibition of salivary amylase

activity. The presence of glucan produced by immobilized GtfD did not further reduce amylase activity. The amount of amylase adsorbed on to hydroxyapatite beads was reduced when salivary amylase was added simultaneously with any of the Gtf enzymes, suggesting that amylase and Gtfs may compete with each other for binding sites on hydroxyapatite. Starch hydrolysates produced by SHA-surface-bound salivary amylase were tested for their effect on glucan production from sucrose by Gtf enzymes in solution and on SHA beads; glucan production by SHA-immobilized GtfB was stimulated in the presence of starch hydrolysates. Glucan synthesized by SHA-immobilized GtfB in the presence of starch hydrolysates was less susceptible to hydrolysis by the fungal enzyme mutanase than was glucan made by SHA-immobilized GtfB in the absence of starch hydrolysates. Glucan production by GtfB associated with ***streptococci*** immobilized on to SHA was also enhanced in the presence of starch hydrolysates. The adhesion of oral micro-organisms to SHA coated with glucan made in the presence and absence of starch hydrolysates was investigated, and some bacteria displayed higher adhesion activities for the glucan made in the presence of the hydrolysates. Therefore, the interaction of amylase and Gtf enzymes on a SHA surface may modulate the formation of glucan and the adherence of oral micro-organisms.

L8 ANSWER 19 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

6

AN 1996:76921 BIOSIS

DN PREV199698649056

TI Immunologic characteristics of a ***Streptococcus*** mutans
glucosyltransferase ***B*** sucrose-binding site
peptide-cholera toxin B-subunit chimeric protein.

AU Laloi, Patrick; Munro, Cindy L.; Jones, Kevin R.; Macrina, Francis L. (1)

CS (1) Box 980678 MCV, Virginia Commonwealth Univ., Richmond, VA 23298-0678
USA

SO Infection and Immunity, (1996) Vol. 64, No. 1, pp. 28-36.

ISSN: 0019-9567.

DT Article

LA English

AB ***Glucosyltransferases*** (Gtfs) produced by the mutans
streptococci are recognized as virulence factors in dental caries,
and the inhibition of Gtfs by secretory immunoglobulin A is predicted to
provide protection against this disease. The basis of such mucosal
immunity is linked to the ability to reliably stimulate production of
secretory immunoglobulin A against Gtfs. In this regard, we are exploring
the immunogenicities of various Gtf peptides genetically fused to the B
subunit of cholera toxin (CTB), a known mucosal adjuvant. In this work, we
have created a gene fusion linking the GtfB active-site (AS) peptide
DANFDSIRVDAVDNDADLLQIA to the amino terminus of CTB. This sequence,
deduced from the nucleotide sequence of gtfB from ***Streptococcus***
mutans GS5, has been found to be strongly conserved in Gtfs from several
mutans ***streptococci***. We have purified this recombinant protein
(AS:CTB) from Escherichia coli carrying the fusion gene under the control
of the lactose operon promoter. This protein was immunogenic in rabbits
and produced specific serum antibodies against both the Gtf peptide and
the CTB moiety. The antiserum was tested for its ability to inhibit GtfB
activity obtained from a mutant of S. mutans able to make only this enzyme
and none of the other usual Gtfs or fructosyltransferase. Approximately
50% of the GtfB activity was inhibited in such assays. These results

suggest that the AS of this enzyme is accessible to antibody binding and that this region of the protein may be considered a vulnerable target for vaccine design and development. The AS:CTB was able to bind GM-1 ganglioside in enzyme-linked immunosorbent assays, indicating that the recombinant protein retained this property, which is thought to be critical to the mucosal immunoadjuvant properties of CTB. Thus, this protein may be promising as a candidate anticaries vaccinogen alone or in combination with other Gtf peptides or conjugates.

L8 ANSWER 20 OF 31 CAPLUS COPYRIGHT 2002 ACS

AN 1996:52031 CAPLUS

DN 124:110588

TI Characterization of ***glucosyltransferase*** ***B***, GtfC, and GtfD in solution and on the surface of hydroxyapatite

AU Venkitaraman, A. R.; Vacca-Smith, A. M.; Kopec, L. K.; Bowen, W. H.

CS Department of Dental Research, University of Rochester Medical Center, Rochester, NY, 14642, USA

SO J. Dent. Res. (1995), 74(10), 1695-701

CODEN: JDREAF; ISSN: 0022-0345

DT Journal

LA English

AB ***Glucosyltransferase*** ***B***, GtfC, and GtfD were purified by hydroxyapatite column chromatog., followed by ultrafiltration from the culture supernatant fluids of 3 ***Streptococcus*** milleri constructs (gift from Dr. H. K. Kuramitsu) which harbored individual gtf genes of ***Streptococcus*** mutants GS5. GtfB, GtfC, and GtfD were enzymically active both in soln. and in an exptl. pellicle (HA-CWS-Gtf) formed by adsorbing Gtf onto the surface of clarified human whole saliva (CWS)-coated hydroxyapatite (HA). The Km values for sucrose for all 3 enzymes were lower when the enzyme was adsorbed to a surface, compared with when it was in soln. In soln. phase assays, and in the absence of primer dextran, glucan prodn. was enhanced 75% when both GtfB and GtfD were present in the reaction mixt., compared with the sum of the individual enzyme activities. This enhancement did not occur when GtfC was addnl. present, or when the GtfB + GtfD enzyme pair was adsorbed onto HA-CWS. In addnl. expts., glucan formed by GtfB or GtfC, but not by GtfD, on a HA-CWS-Gtf surface increased adherence of ***Streptococcus*** mutants GS5 and ***Streptococcus*** sobrinus 6715 by 7- to 9-fold compared with adherence when no glucan was present on the pellicle surface. Further, treatment of the HA-CWS-GtfB-glucan or HA-CWS-GtfC-glucan pellicle with .alpha.-1,6-dextranase significantly reduced adherence of both ***streptococcal*** strains. These results show that GtfB, GtfC, and GtfD are enzymically active in an adsorbed state and that the nature of their product glucan can influence the adherence of cariogenic oral ***streptococci*** to an exptl. pellicle.

L8 ANSWER 21 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1997:304801 BIOSIS

DN PREV199799612604

TI Purification of ***glucosyltransferases*** (GtfB/C and GtfD) from mutant strains of ***Streptococcus*** mutants.

AU Chia, Jean-San; Hsieh, Chi-Chuan; Yang, Czaui-Siung; Chen, Jen-Yang (1)

CS (1) Dep. Bacteriol., Sch. Dentistry, College Med., National Taiwan Univ., Taipei Taiwan

SO Chinese Journal of Microbiology and Immunology (Taipei), (1995) Vol. 28,

No. 1, pp. 1-12.
ISSN: 0253-2662.

DT Article
LA English
SL English; Chinese

AB ***Streptococcus*** mutans expresses three glucotransferases (GTFs), i.e., GtfB, GtfC, and GtfD, which synthesize glucan polymers from sucrose. Two genetically constructed mutants of *S. mutans* which stably expressed either the cell-associated or the extracellular GTFs were selected for purification and characterization of these enzymes. The cell-associated GtfB and GtfC from the strain GS-5DD lacking the *gtfD* gene expression were extracted by urea, renatured by dialysis in sodium phosphate buffer and then separated from the other wall-associated components by column chromatography. The extracellular GtfD was purified from the culture supernatant of strain NHS1 lacking *gtfB* and *gtfC* gene expression. The molecular weights of the purified GTFs was similar (150-160 kDa), as determined by SDS-polyacrylamide gel electrophoresis. The GtfB/C preparation synthesized primarily water-insoluble glucan in a primer independent manner. However, the presence of the dextran enhanced the enzymatic activities of the GtfB/C. GtfD synthesized water-soluble glucan exclusively in a primer dependent manner. Purified GtfD had a pH optimum of 5.5, and a K_m value of 4.35 mM for sucrose. These results indicated that the mutated strains served as an efficient and specific host to obtain native GTFs.

L8 ANSWER 22 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

7

AN 1993:141358 BIOSIS

DN PREV199395074158

TI Comparative effectiveness of the cholera toxin B subunit and alkaline phosphatase as carriers for oral vaccines.

AU Dertzbaugh, Mark T. (1); Elson, Charles O.

CS (1) US Army Med. Res. Inst. Infect. Dis., Frederick, MD 21702-5011

SO Infection and Immunity, (1993) Vol. 61, No. 1, pp. 48-55.

ISSN: 0019-9567.

DT Article

LA English

AB The purpose of this study was to determine whether the B subunit of cholera toxin (CtxB) has adjuvant activity over and above serving as a carrier protein for orally administered vaccines. An oligonucleotide that encodes an antigenic determinant (GtfB.1) from the ***glucosyltransferase*** ***B*** gene (*gtfB*) of ***Streptococcus*** mutans was genetically fused to the 5' terminus of either the CtxB gene (*ctxB*) or the *Escherichia coli* alkaline phosphatase gene (*phoA*). The resulting chimeric proteins were expressed in a *phoA* mutant strain of *E. coli* and then purified. The antigenicities of the proteins were confirmed by immunoblotting analysis using antisera specific for GtfB, CtxB, or PhoA. An equimolar amount of peptide on each carrier was administered by gastric intubation to mice three times at 10-day intervals. Antibody titers to the peptide, CtxB, and PhoA (in the serum, intestine, vagina, saliva, and bronchus) were determined by enzyme immunoassay. Antibody to the peptide was detected only in the sera of mice immunized with the peptide fused to CtxB. No anti-peptide antibody was detected in mice immunized with the peptide fused to PhoA. The lack of detectable levels of anti-peptide antibody in intestinal lavage fluid was

attributed to dilution of the sample beyond the sensitivity of the assay.
 This was confirmed by cultivation of Peyer's patch and mesenteric lymph
 node tissue from mice orally immunized with the GtfB.1::CtxB chimera.
 Using this method, antipeptide antibody was detected in the culture fluid.
 We conclude that CtxB possesses unique properties that allow it to act as
 more than a simple carrier protein.

L8 ANSWER 23 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1992:270440 BIOSIS
 DN BR42:129390
 TI COMPARISON OF THE ORAL IMMUNOGENICITY OF A FOREIGN PEPTIDE WHEN COUPLED TO
 CHOLERA TOXIN B SUBUNIT OR TO ALKALINE PHOSPHATASE.
 AU DERTZBZUGH M T; ELSON C O
 CS UNIV. ALABAMA BIRMINGHAM, BIRMINGHAM, ALA. 35294.
 SO MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY
 (FASEB), PART 1, ANAHEIM, CALIFORNIA, USA, APRIL 5-9, 1992. FASEB (FED AM
 SOC EXP BIOL) J. (1992) 6 (4), A1229.
 CODEN: FAJOEC. ISSN: 0892-6638.
 DT Conference
 FS BR; OLD
 LA English

L8 ANSWER 24 OF 31 CAPLUS COPYRIGHT 2002 ACS
 AN 1991:576713 CAPLUS
 DN 115:176713
 TI Recombinant cholera toxin-antigenic peptide fusion proteins and their use
 as vaccines
 IN Dertzbaugh, Mark T.; Macrina, Francis L.
 PA Center for Innovative Technology, USA
 SO PCT Int. Appl., 68 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9107979	A1	19910613	WO 1990-US6811	19901128
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2069106	AA	19910530	CA 1990-2069106	19901128
EP 502099	A1	19920909	EP 1991-900482	19901128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05503420	T2	19930610	JP 1991-501085	19901128
PRAI US 1989-442783		19891129		
WO 1990-US6811		19901128		

AB Recombinant fusion proteins comprising an antigen epitope linked to the
 N-terminus of a cholera toxin B subunit fragment are produced. These may
 be used as vaccines. A chimeric gene contg. the ompA signal sequence, a
 fragment of the ***glucosyltransferase*** ***B*** gene (gtfB) of
 Streptococcus mutans, and a part of the ctxB gene was constructed
 and expressed in Escherichia coli. Antisera to the fusion protein
 produced by these transformants inhibited the S. mutans enzyme in vitro.
 This recombinant protein is proposed as a vaccine against dental caries.

L8 ANSWER 25 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

AN 1990:354476 BIOSIS

DN BA90:51055

TI INHIBITION OF ***STREPTOCOCCUS*** -MUTANS ***GLUCOSYLTRANSFERASE***
ACTIVITY BY ANTISERUM TO A SUBSEQUENCE PEPTIDE.

AU DERTZBAUGH M T; MACRINA F L

CS DEP. MICROBIOLOGY IMMUNOLOGY, VIRGINIA COMMONWEALTH UNIVERSITY, RICHMOND,
VA. 23298-0678.

SO INFECT IMMUN, (1990) 58 (6), 1509-1513.

CODEN: INFIBR. ISSN: 0019-9567.

FS BA; OLD

LA English

AB An antigenic 15-amino-acid peptide sequence (gtfB.1) from the
glucosyltransferase ***B*** enzyme of the cariogenic bacterium
Streptococcus mutans GS-5 was identified previously from the
genetic fusion of this sequence to the B subunit of chlorea toxin. The
resulting chimeric protein was used to raise antiserum in rabbits. This
antiserum was shown to recognize the native ***glucosyltransferase***
enzyme and to inhibit its activity. The antiserum inhibited the synthesis
of water-soluble glucan by .apprx. 40% and the synthesis of
water-insoluble glucan by > 90%. The antiserum was shown to partially
inhibit fructosyltransferase activity as well. The ability of this
antipeptide antiserum to inhibit several enzymes from S. mutans suggests
that these enzymes share an epitope related to enzymatic activity.

L8 ANSWER 26 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

AN 1990:133316 BIOSIS

DN BA89:72127

TI REGULATION OF EXPRESSION OF ***STREPTOCOCCUS*** -MUTANS GENES IMPORTANT
TO VIRULENCE.

AU HUDSON M C; CURTISS R III

CS DEP. BIOL., WASHINGTON UNIV., ST. LOUIS, MISS. 63130.

SO INFECT IMMUN, (1990) 58 (2), 464-470.

CODEN: INFIBR. ISSN: 0019-9567.

FS BA; OLD

LA English

AB Studies were initiated to investigate the regulation of
Streptococcus mutans genes which are believed to be important to
virulence. Operon fusions were constructed between S. mutans gene
regulatory regions and a promoterless chloramphenicol acetyltransferase
gene (cat) found on the plasmid pMH109. Specifically, fusions were
generated between cat and the S. mutans genes encoding
fructosyltransferase (ftf) and the ***glucosyltransferase*** ***B***
/C (gtfB/C) operon. Constructs were confirmed by restriction enzyme
analysis, and the fusions were subcloned into the integration vehicle
pVA891. Following generation of multimeric DNA, recombinant plasmids were
introduced into the S. mutans genome by Campbell-type insertion, resulting
in single-copy operon fusions. Chloramphenicol acetyltransferase specific
activities were used to monitor the expression of the S. mutans gtfB/C
operon and ftf determinants. The expression of these genes is increased by
the presence of sucrose and is followed by a rapid decline in expression
over time. Additionally, expression of the gtfB/C operon is increased in
S. mutans cells bound to artificial tooth pellicles.

L8 ANSWER 27 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

10

AN 1990:89392 BIOSIS

DN BA89:48743

TI CHOLERA TOXIN B-SUBUNIT GENE FUSION STRUCTURAL AND FUNCTIONAL ANALYSIS OF THE CHIMERIC PROTEIN.

AU DERTZBAUGH M T; PETERSON D L; MACRINA F L

CS DEP. MICROBIOL. IMMUNOL., VIRGINIA COMMONWEALTH UNIV., RICHMOND, VA. 23298.

SO INFECT IMMUN, (1990) 58 (1), 70-79.

CODEN: INFIBR. ISSN: 0019-9567.

FS BA; OLD

LA English

AB A synthetic peptide, encoding amino acid residues 345 to 359 of the ***glucosyltransferase*** ***B*** enzyme of ***Streptococcus*** mutans GS-5, was genetically fused to the N-terminal end of the B-subunit gene of cholera toxin. The protein was overexpressed in Escherichia coli and retained the antigenicity associated with cholera toxin B subunit (CTB) as well as that associated with ***glucosyltransferase*** ***B***. The addition of 15 amino acids to the N-terminal end of CTB did not appear to affect the gross structure of the protein significantly. The chimeric protein monomers assembled into a functional oligomer which exhibited only minor conformational differences from native CTB as measured by circular dichroism. The chimera bound to GM1 ganglioside and thus retained the biological activity of CTB. These results demonstrate that genetic fusion of small peptides to the N terminus of CTB has only a minimal effect on the structure and function of the protein. Furthermore, the chimera was shown to be immunogenic when fed to mice. This work has important implications in the construction of CTB chimeras for use as oral vaccines.

L8 ANSWER 28 OF 31 CAPLUS COPYRIGHT 2002 ACS

AN 1992:52794 CAPLUS

DN 116:52794

TI Chimeric proteins constructed by gene fusion: an approach to vaccination against oral ***streptococci***

AU Dertzbaugh, Mark Thomas

CS Virginia Commonw. Univ., Richmond, VA, USA

SO (1989) 117 pp. Avail.: Univ. Microfilms Int., Order No. DA9122333

From: Diss. Abstr. Int. B 1991, 52(3), 1234

DT Dissertation

LA English

AB Unavailable

L8 ANSWER 29 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

11

AN 1990:26851 BIOSIS

DN BA89:13817

TI PLASMID VECTORS FOR CONSTRUCTING TRANSLATIONAL FUSION TO THE B SUBUNIT OF CHOLERA TOXIN.

AU DERTZBAUGH M T; MACRINA F L

CS DEP. MICROBIOL. IMMUNOL., VA. COMMONWEALTH UNIV., RICHMOND, VA. 23298-0678.

SO GENE (AMST), (1989) 82 (2), 335-342.

CODEN: GENED6. ISSN: 0378-1119.

FS BA; OLD

LA English

AB A family of plasmid cloning vectors has been developed for creating translational fusions to the ctxB gene encoding the B subunit of cholera toxin (CTB) in Escherichia coli. These vectors permit insertion of transcriptionally and translationally competent gene sequences upstream from ctxB. To test the utility of the system, a portion of the ***glucosyltransferase*** ***B*** (GTF) gene (gtfB) from the cariogenic bacterium ***Streptococcus*** mutans GS-5 (Bratthall serotype c), encoding the N-terminal one-third of the protein, was inserted into each vector. E. coli lysates containing the constructs were partially purified by passage over a GM1 ganglioside affinity column. Western blotting analysis of the column retentate from one of the lysates revealed the presence of a novel 58-kDa protein which cross-reacted with antisera to GTF and CTB. These vectors are of general use for making other translational fusions to ctxB. The high binding affinity of CTB can be exploited in purifying large polypeptides fused to this relatively small protein. Moreover, these vectors can be used to create neoantigens with altered immunogenicity for use in polypeptide-based vaccines.

L8 ANSWER 30 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1989:374904 BIOSIS

DN BR37:54027

TI GENETIC FUSION OF A PEPTIDE FROM ***STREPTOCOCCUS*** -MUTANS ***GLUCOSYLTRANSFERASE*** ***B*** TO CHOLERA TOXIN B SUBUNIT STRUCTURE AND IMMUNOGENICITY.

AU DERTZBAUGH M; MACRINA F

CS VA. COMMONW. UNIV., RICHMOND, VA 23298-0678, USA.

SO 89TH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR MICROBIOLOGY, NEW ORLEANS, LOUISIANA, USA, MAY 14-18, 1989. ABSTR ANNU MEET AM SOC MICROBIOL. (1989) 89 (0), 128.

CODEN: ASMACK. ISSN: 0094-8519.

DT Conference

FS BR; OLD

LA English

L8 ANSWER 31 OF 31 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
12

AN 1979:161556 BIOSIS

DN BA67:41556

TI ANTIGENIC RELATIONSHIPS BETWEEN THE GLUCOSYL TRANSFERASE ACTIVITIES OF ***STREPTOCOCCUS*** -MUTANS-SSP-MUTANS.

AU KURAMITSU H K; INGERSOLL L

CS DEP. MICROBIOL. IMMUNOL., NORTHWEST. UNIV. MED. DENT. SCH., CHICAGO, ILL. 60611, USA.

SO ARCH ORAL BIOL, (1978) 23 (8), 691-696.

CODEN: AOBIAR. ISSN: 0003-9969.

FS BA; OLD

LA English

AB Antibodies, directed against the partially-purified ***glucosyltransferase*** -A (synthesizing primarily insoluble glucans) and purified ***glucosyltransferase*** - ***B*** (producing predominantly soluble glucans) of S. mutans GS5 (serotype c), were used to assess the antigenic relatedness of the corresponding enzyme activities of strains MT703 (serotype e) and OMZ-175 (serotype f). Anti-GTF-A and

anti-GTF-B inhibited the corresponding activities from strains GS5, MT703 and OMZ-175 equally well. The cell-associated activities and sucrose-dependent adherence capabilities of all 3 organisms were strongly inhibited in a similar way by anti-GTF-A. The adherence-inhibiting activity of anti-GTF-A was demonstrated to be directed against a heat-sensitive component of the cell surface, probably the cell-associated GTF activity. The results are discussed in terms of the previously proposed close genetic relationship between *S. mutans* serotype c, e and f organisms.

=> s (aspartate 562)

L9 1 (ASPARTATE 562)

=> d bib ab kwic

L9 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1995:351731 BIOSIS

DN PREV199598366031

TI Characterization of chitin synthase 2 of *Saccharomyces cerevisiae*:

Implication of two highly conserved domains as possible catalytic sites.

AU Nagahashi, Shigehisa; Sudoh, Masayuki; Ono, Naomi; Sawada, Rumi; Yamaguchi, Emi; Uchida, Yukiko; Mio, Toshiyuki; Takagi, Masamichi; Arisawa, Mikio; Yamada-Okabe, Hisafumi (1)

CS (1) Dep. Mycol., Nippon Roche Research Cent., 200 Kajiwara, Kamakura, Kanagawa 247 Japan

SO Journal of Biological Chemistry, (1995) Vol. 270, No. 23, pp. 13961-13967.
ISSN: 0021-9258.

DT Article

LA English

AB Chitin synthase 2 of *Saccharomyces cerevisiae* was characterized by means of site-directed mutagenesis and subsequent expression of the mutant enzymes in yeast cells. Chitin synthase 2 shares a region whose sequence is highly conserved in all chitin synthases. Substitutions of conserved amino acids in this region with alanine (alanine scanning) identified two domains in which any conserved amino acid could not be replaced by alanine to retain enzyme activity. These two domains contained unique sequences, Glu-561-Asp-562 Arg-563 and Gln-601-Arg-602-Arg-603-Arg-604-Trp-605, that were conserved in all types of chitin synthases. Glu-561 or arginine at 563, 602, and 603 could be substituted by glutamic acid and lysine, respectively, without significant loss of enzyme activity. However, even conservative substitutions of Asp-562 with glutamic acid, Gln-601 with asparagine, Arg-604 with lysine, or Trp-605 with tyrosine drastically decreased the activity, but did not affect apparent K_m values for the substrate significantly. In addition to these amino acids, Asp-441 was also found in all chitin synthase. The mutant harboring a glutamic acid substitution for Asp-441 severely lost activity, but it showed a similar apparent K_m value for the substrate. Amounts of the mutant enzymes in total membranes were more or less the same as found in the wild type. Furthermore, Asp-441, Asp-562, Gln-601, Arg-604, and Trp-605 are completely conserved in other proteins possessing N-acetylglucosaminyltransferase activity such as NodC proteins of *Rhizobium* bacteria. These results suggest that Asp-441, Asp-562, Gln-601, Arg-604, and Trp-605 are located in the active pocket and that they function as the catalytic residues of the enzyme.

IT Miscellaneous Descriptors

ARGININE-604; ASPARTATE-441; ***ASPARTATE*** - ***562*** ;
GLYCINE-601; STRUCTURE-ACTIVITY RELATIONSHIP; TRYPTOPHAN-605

=> s (aspartate 567)

L10 1 (ASPARTATE 567)

=> d bib ab kwic

L10 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:266934 BIOSIS

DN PREV200100266934

TI Overexpression of the human Asp567Gly FSH receptor in transgenic mice.

AU Simoni, M. (1); Gromoll, J. (1); Nordhoff, V. (1); Schlatt, S. (1);

Foppiani, L. (1); Nieschlag, E. (1)

CS (1) Institute of Reproductive Medicine of the University, Muenster Germany

SO Journal of Andrology, (May June, 2001) No. Supplement, pp. 204. print.

Meeting Info.: VIIth International Congress of Andrology Montreal, Canada

June 15-19, 2001

ISSN: 0196-3635.

DT Article; Conference

LA English

SL English

IT . . .

Systems of Organisms

serum: blood and lymphatics; testicles: histology, reproductive system;

testis: reproductive system

IT Chemicals & Biochemicals

FSH; human ***aspartate*** - ***567*** -glycine FSH receptor:

overexpression; testosterone

=> s (histidine 561)

L11 0 (HISTIDINE 561)

=> s (tryptophan 491)

L12 0 (TRYPTOPHAN 491)

=> s (glutamate 489)

L13 0 (GLUTAMATE 489)

=> s (aspartate 586)

L14 0 (ASPARTATE 586)

=> s (aspartate 591)

L15 0 (ASPARTATE 591)

=> s (histidine 585)

L16 0 (HISTIDINE 585)

=> s (tryptophan 517)

L17 0 (TRYPTOPHAN 517)

=> s (glutamate 515)

L18 1 (GLUTAMATE 515)

=> s (tyrosine 587)

L19 4 (TYROSINE 587)

=> d 118 bib ab kwic

L18 ANSWER 1 OF 1 USPATFULL

AN 2000:64865 USPATFULL

TI 5,6,7,8-tetrahydropyrido[2,3-D]pyrimidines

IN Taylor, Edward C., Princeton, NJ, United States

Shih, Chuan, Carmel, IN, United States

Lee, Koo, Taejon, Korea, Republic of

Gossett, Lynn S., Indianapolis, IN, United States

PA The Trustees of Princeton University, Princeton, NJ, United States (U.S. corporation)

Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

PI US 6066639 20000523

WO 9741115 19971106

AI US 1999-171772 19990226 (9)

WO 1996-US14822 19960917

19990226 PCT 371 date

19990226 PCT 102(e) date

PRAI US 1996-21174P 19960501 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Balasubramanian, V

LREP Mathews, Collins, Shepherd & Gould, P.A.

CLMN Number of Claims: 15

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1137

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Glutamic acid derivatives in which the amino group is substituted with a 2-amino-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-6-ylalkyl-Z-carbonyl group, in which Z is a divalent, five-membered, nitrogen-containing heterocyclic ring system optionally containing a sulfur or nitrogen atom as a second hetero ring member, are antineoplastic agents. A typical embodiment is N-{3-[2-(2-amino-4-hydroxy-5,6,7,8-tetrahydropyrido[2,3-d]pyrimidin-6-yl)ethyl]-pyrazol-5-ylcarbonyl}-L-glutamic acid.

DETD . . . Cl.sub.2 (35 mg, 0.05 mmol), cuprous iodide (19 mg, 0.1 mmol), triethylamine (0.7 mL), and acetonitrile (50 mL) yield dimethyl N-(2-[2-(2-pivaloylamino-4-hydroxypyrido[2,3-d]pyrimidin-6-yl)ethynyl]-1-triphenylmethylimidazol-4-ylcarbonyl)-L- ***glutamate*** [***515*** mg, 66% after flash column chromatography (ethyl acetate:hexanes, 2:1), mp 93-95.degree. C]: .sup.1 H NMR (CDCl.sub.3) .delta. 12.05 (br s, .

=> dup rem l19

PROCESSING COMPLETED FOR L19

L20 3 DUP REM L19 (1 DUPLICATE REMOVED)

=> d bib ab kwic 1-

YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L20 ANSWER 1 OF 3 USPATFULL

AN 1999:27847 USPATFULL

TI Mice mutant for functional Fc receptors and method of treating autoimmune diseases

IN Ravetch, Jeffrey V., New York, NY, United States

Takai, Toshiyuki, Okayama, Japan

Sylvestre, Diana, New York, NY, United States

Clynes, Raphael, New York, NY, United States

PA Sloan Kettering Institute for Cancer Research, New York, NY, United States (U.S. corporation)

PI US 5877396 19990302

AI US 1994-292569 19940818 (8)

RLI Continuation-in-part of Ser. No. US 1993-52267, filed on 23 Apr 1993, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Stanton, Brian R.

LREP White, John P.

CLMN Number of Claims: 18

ECL Exemplary Claim: 1

DRWN 112 Drawing Figure(s); 48 Drawing Page(s)

LN.CNT 3545

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed herein is a non-naturally occurring non-human vertebrate animal incapable of expressing a functional Fc receptor which may optionally be capable of expressing a protein which comprises a domain of a human Fc receptor, as well as DNA encoding such Fc receptor-based proteins. Also disclosed are in vivo methods for identifying proinflammatory agents that depend on a functional Fc receptor, in vivo methods for identifying proinflammatory agents that do not depend on a functional Fc receptor, and both in vivo and in vitro methods of identifying anti-inflammatory agents. Pharmaceutical compositions containing, and methods of treating inflammation with anti-inflammatory agents are also described.

DRWD . . . cytoplasmic domains of the chimeric .mu. chain are derived from wild-type .mu. chain, mutated transmembrane .mu. chain (replacement of both ***tyrosine*** ***587***, and serine 588 with valine) and murine cytoplasmic Ig-.alpha. (amino acids 160-220), respectively. IgM/Ig-.beta. is the same as IgM/Ig-.alpha. except. . .

L20 ANSWER 2 OF 3 USPATFULL

AN 1998:128081 USPATFULL

TI Method for screening for targets for anti-inflammatory or anti-allergic agents

IN Ravetch, Jeffrey V., New York, NY, United States

Kurosaki, Tomohiro, Fort Lee, NJ, United States

PA Sloan-Kettering Institute for Cancer Research, New York, NY, United States (U.S. corporation)

PI US 5824487 19981020

AI US 1995-542686 19951013 (8)

RLI Continuation of Ser. No. US 1993-52269, filed on 23 Apr 1993, now

abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Schwadron, Ronald B.

LREP White, John P.

CLMN Number of Claims: 9

ECL Exemplary Claim: 1

DRWN 44 Drawing Figure(s); 20 Drawing Page(s)

LN.CNT 1004

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a method for identifying a cellular protein capable of specifically binding to an activated antibody receptor, whose cytoplasmic domain comprising an ARH1 motif, comprising (a) obtaining cells comprising receptors having the ARH1 motif; (b) lysing the cells under conditions whereby the native complex of the receptor having the ARH1 motif and the cellular protein is preserved; (c) isolating the complex; and (d) testing the associated receptor and the protein for biochemical activities, thereby identifying the cellular protein capable of specifically binding to an activated antibody receptor, whose cytoplasmic domain comprising an ARH1 motif. This invention further provides a method for identifying a cellular molecule capable of being a target for designing drugs for autoimmune disease, inflammation or allergy which comprises (a) contacting a cell lysate with a molecule having a motif of amino acid sequence, AENTITYSLLKHP under the conditions permitting formation of a complex between the cellular target molecule with the motif; (b) isolating the complex formed in step (a); and (c) testing the complex for biochemical activities, thereby identifying the cellular molecule capable of being a target for designing drugs for autoimmune disease, inflammation or allergy.

DRWD . . . cytoplasmic domains of the chimeric .mu. chain are derived from wild-type .mu. chain, mutated transmembrane .mu. chain (replacement of both ***tyrosine*** ***587***, and serine 588 with valine) and murine cytoplasmic Ig-.alpha. (amino acids 160-220), respectively. IgM/Ig-.beta. is the same as IgM/Ig-.alpha. except. . .

L20 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1

AN 1994:226453 BIOSIS

DN PREV199497239453

TI Point mutations define a mIgM transmembrane region motif that determines intersubunit signal transduction in the antigen receptor.

AU Pleiman, Christopher M.; Chien, Nadine C.; Cambier, John C. (1)

CS (1) Div. Basic Sci., Dep. Pediatrics, Natl. Jewish Cent. Immunol. and Respiratory Med., 1400 Jackson St., Denver, CO 80206 USA

SO Journal of Immunology, (1994) Vol. 152, No. 6, pp. 2837-2844.

ISSN: 0022-1767.

DT Article

LA English

AB Ag binding to the membrane Ig (mIg) substructure of the B cell Ag receptor leads to activation of cytoplasmic effector molecules including blk, fyn, lyn, and/or lck tyrosine kinases that are associated with receptor's dimeric Ig-alpha/Ig-beta transducer substructure. The structural basis of the apparent intermolecular transmission of this information within the receptor complex is unknown. Here we report that conservative point mutation of a sequence, S-584-K-597, at the cytoplasmic end of the predicted transmembrane spanning domain of the mIgM heavy chain (mu)

ablates Ag-activated signal transduction, while having no detectable effect on association of mIgM with Ig-alpha/Ig-beta heterodimers. Specifically, mutation of serine-584 to alanine, ***tyrosine*** - ***587*** to phenylalanine, threonine-592 to valine, or lysine-597 to isoleucine completely abrogated Ag-induced signal transduction leading to protein tyrosine phosphorylation and Ca-2+ mobilization. Interestingly, mutants in the more peripheral of these residues, serine-584 to alanine and lysine-597 to isoleucine, remained responsive to a monoclonal antireceptor Ab (b-7-6) and all mutants remained responsive to polyclonal antireceptor Ab. These data implicate the polar sequence, -Y-587STTVT-592-, in transfer of information from ligand binding to transducer substructures within this heterooligomeric receptor complex. They further indicate that receptor activation by ligands that bind with high affinity and/or to constant region mIg epitopes is less dependent on the integrity of this motif.

AB. . . signal transduction, while having no detectable effect on association of mIgM with Ig-alpha/Ig-beta heterodimers. Specifically, mutation of serine-584 to alanine, ***tyrosine*** - ***587*** to phenylalanine, threonine-592 to valine, or lysine-597 to isoleucine completely abrogated Ag-induced signal transduction leading to protein tyrosine phosphorylation and. . .